EXHIBIT DX1

TO DECLARATION OF MARY S. YOUNG IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE OPINIONS AND TESTIMONY OF RICHARD WENZEL, M.D.

Report Prepared for Blackwell Burke

In re Bair Hugger Forced Air Warming Devices Products Liability Litigation

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Outline of the Report

I. Anesthesia, cooling body temperatures (hypothermia) and the associated adverse events

The normal body temperature in healthy people is 98.6° F or 37° C. There is little fluctuation during the day because of the body's sophisticated thermostat, located in the brain, which maintains a relatively constant temperature. This is good because the body's chemistry works best at 37 ° C.

Hypothermia is defined at <36 ° C (< 96.8° F), when measured in deep tissue ("core" temperature). With anesthesia the body's core temperature (chest, abdomen, brain and spinal cord) drops, and there is a failure of the thermostat's regulation to normalize the temperature (red line in figure 1).

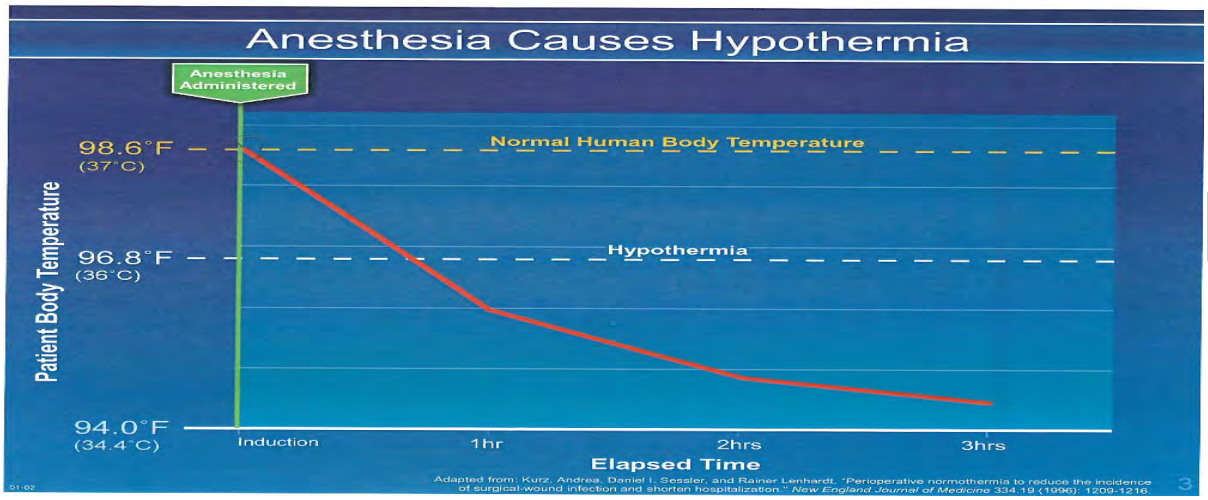
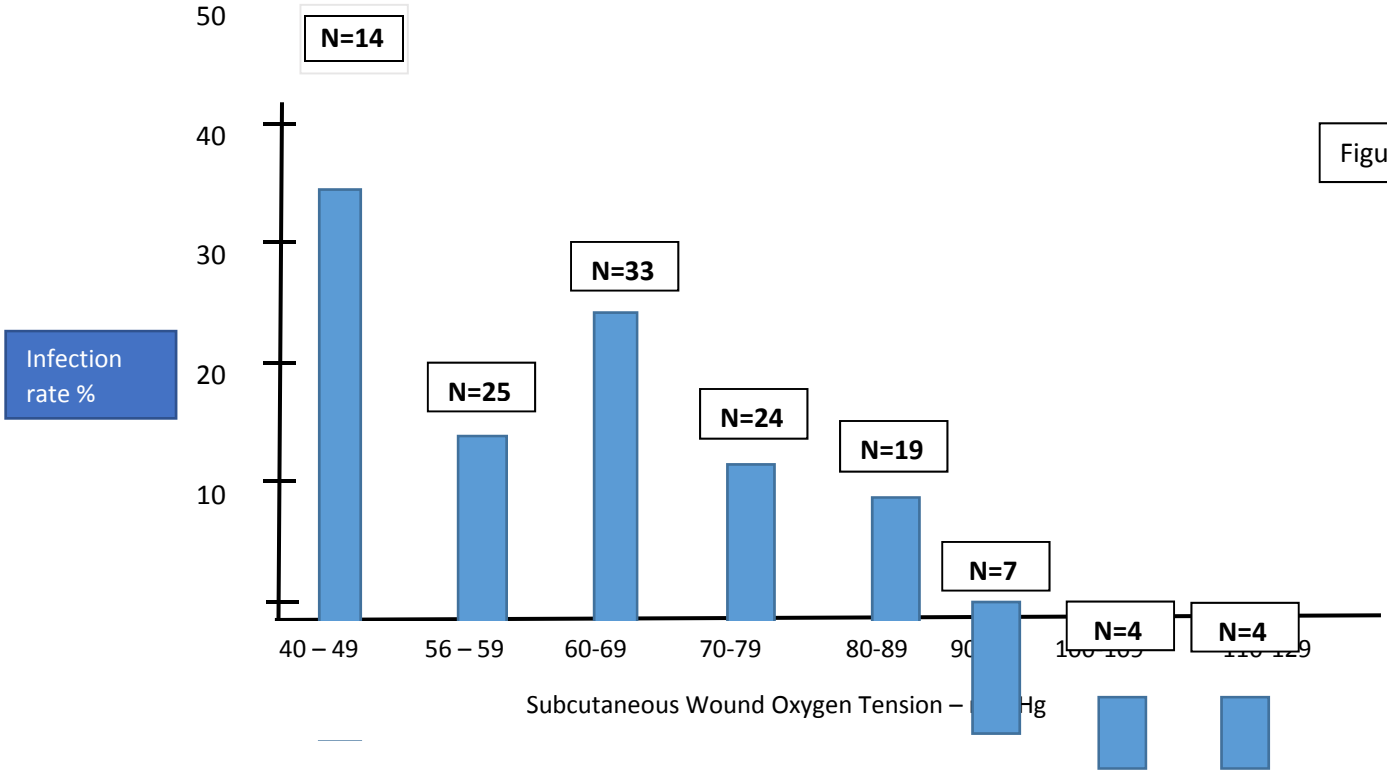


Figure 1

The body's response to the stress of hypothermia is an outpouring of the stress hormone, norepinephrine, causing constriction of the arterial blood supply to the subcutaneous tissue (just below the skin), essentially a decrease in blood perfusion right at the operative site. The reduced blood supply in turn means that there is a reduced oxygen tension at the subcutaneous area, and a resulting sluggish response of white cells responding to nearby bacteria, to their engulfment of the bacteria, and to their killing of bacteria. Furthermore, the perioperative antibiotics - administered to reduce the risk of a surgical site infection - do not work as well in lower oxygen states. (Hart S. R. et al. Unintended perioperative hypothermia. *The Ochsner Journal* 2011; 11: 259-70; Kasai T et al. Preoperative blood pressure and catecholamines related to hypothermia during general anesthesia. *Acta Anesthesial Scand* 2003; 47: 208 – 12; Sesssler D.I. et al. Non-Pharmacologic prevention of surgical wound infection. *Anesthesial Clin* 2006; 24: 279-97).

The physiological response to hypothermia has been linked to important outcomes in surgical patients. Clinical studies have shown that the lower the oxygen tension of the subcutaneous tissue, the greater the surgical site infection risk. In a prospective observational study of 130 surgical patients, Harriet Williams Hopf and colleagues showed an inverse relationship between subcutaneous wound oxygen tension and surgical site infection rate (Figure 2): if the oxygen tension was as low as 40-49 mm Hg, the infection rate was over 40%, but the SSI rate fell to zero if the oxygen tension was ≥90 mm Hg. (Hopf et. Al, Wound Tissue Oxygen Tension Predicts the Risk of Wound Infection in Surgical Patients, Arch Surg 1997, 32:997-1004)



Infection rate is inversely proportional to maximum subcutaneous wound oxygen tension (Psq O2 max) ($p < 0.01$, X2 contingency table)

Hopf, et a.l Arch Surg 1997; 132:997-1004

This figure shows the high proportion of general surgery patients whose subcutaneous wound oxygen tension was low and who were at risk for a SSI in the pre-warming era. Hypothermia during surgery has not only been linked to increased risk of wound infection but also increased risk of morbid cardiac events, a need for more blood transfusions, complications of major surgery and post-operative shivering (Eileen Scott. A systematic review of intraoperative warming to prevent post-operative complications. AORN Journal 2006; 83: 1090 – 1113).

The CDC classifies wound infections as “superficial” if they involve skin and subcutaneous tissue and “deep” if they involve “fascia or muscle”. An organ/space SSI involves any part of the body deeper than facial muscle and was opened or manipulated during the operative procedure.

Post-operative pain has also been linked to elevated stress hormone levels’ associated arteriolar vasoconstriction, and decreased tissue oxygen pressure. Akca and colleagues hypothesized that patients undergoing knee surgery would have less pain and higher subcutaneous tissue oxygen levels if the knee was injected at the end of surgery with lidocaine vs saline. 30 adult patients were randomized, and over the following hour and a half, the placebo group had a mean subcutaneous oxygen level of 86 mmHg vs 113mm in the lidocaine group ($p=0.016$), and the mean pain score (on a 1-100 visual analogue) was 40 in the placebo group vs 11 in the lidocaine group ($p < 0.001$). The authors suggest that “control of postoperative pain is a major determinant of surgical site infection,” citing the work of Hopf et al. (See Akca et al., Postoperative pain and subcutaneous oxygen tension. *Lancet*. 1999; 354: 41-42).

Both studies are consistent with the concept that stress from anesthesia or of pain is linked to reduced subcutaneous oxygen pressures, known to influence surgical site infection rates. Furthermore,

warming increases subcutaneous oxygen tension: Ikeda and colleagues used a radiant heater applied locally to 10 volunteers and measured subcutaneous oxygen tension. At 38^{o} C, 42^{o}C and 46^{o}C, oxygen tension increased approximately 50% during heating to comparable levels at all three temperatures tested. Of interest, subcutaneous oxygen tension remained elevated for 3 hours after heating was discontinued. (Ikeda et al., Local Radiant Heating Increases Subcutaneous Oxygen Tension, *Am J Surg* 1998; 175: 33-37)

II. Benefits of avoiding hypothermia, Forced Air Warming and the Bair Hugger Device

Fortunately the adverse events linked to anesthesia, the associated hypothermia and reduced tissue oxygenation can be reversed with warming of the surgical patient, maintaining a core body temperature greater than 36° C (96.8° F). Most studies have been performed with forced air warming devices and most of the latter with the Bair Hugger.

a. Prospective, Randomized, Controlled Clinical Trials

i. Andrea Kurz and colleagues randomized 200 colorectal surgery patients to the use of a Bair Hugger patient warming system during the operation or to control (no warming). The controls had a forced air warmer set to deliver ambient air vs a 40° set point for the warmed group, which also received IV fluids through a warmer. Core temperatures at the end of surgery were significantly lower in controls (34.7 ± 0.6° C) vs the warmed group (36.6 ± 0.5° C). Hospital stay in the infected patients was one week longer than the unifected... "indicating that most infections were substantial." To minimize the decrease in wound perfusion due to pain postoperatively, patients with pain were given opioids. **The surgical site infection rate was 19% in controls vs 6% in the warmed patients.** (Kurz et al., Perioperative Normothermia to Reduce the Incidence of Surgical-Wound Infection and Shorten Hospitalization, *N Engl. J Med* 1996; 19:1209-1216).

In her deposition, Dr. Andrea Kurz was asked if she still thought the data were valid and also if she were to do the study again, what changes would she make? She said that she still believes that "maintenance of normothermia decreases infection risk, but the effect might be closer to 30% reduction or so, which in effect is a humongous, enormously large effect size for any medical intervention" (p. 201). She also said that today she would have a larger study size and emphasized that the control arm would have to be warmed in some fashion for an ethically sound study since "active warming has become standard" (p. 199). The key point is that "due to the fact that patients are warmed, we don't see the significant decrease of hypothermia any more, and therefore in any study the effect size wouldn't be as large as in this particular one" (p. 199).

ii. Andrew Melling and colleagues randomized 421 patients undergoing clean surgery to ≥ 30 minutes of preoperative warming or no warming. All patients were expected to have brief operative times of under 50 minutes. Both Bair Hugger and local warming methods increased core temperatures by .35 and .13° C and had equal outcomes, and their results were pooled and compared to controls with no warming. The mean core temperature after surgery was > 36° C. **The surgical site infection rate was 14% in controls and 5% in warmed patients** (Melling et al., Effects of perioperative warming on the incidence of wound infection after clean surgery: a randomized controlled trial, *Lancet* 2001; 358:876-80).

Both clinical trials used the Bair Hugger and had blinded (masked) evaluators who did not know to which study arm the patients were assigned.

b. *Systematic reviews of controlled clinical trials (meta-analyses).*

Meta-analyses are systematic reviews of ≥ 2 studies, performed to estimate the overall effect of an intervention, since any single study may have a somewhat different outcome than another. Meta-analyses represent the best overall estimate of the intervention.

A meta-analysis was reported by the Cochrane Library in 2016. They included both the Kurz and Melling studies and **estimated the risk ratio for surgical site infections favoring warming at 0.36 (CI_{95} - 0.20-.66), suggesting that 64% of surgical site infections could be eliminated with warming.** (Madrid E et al. Active body surface warming systems for preventing complications caused by inadvertent perioperative hypothermia in adults (Review). (Cochrane database of systematic reviews 2016, Issue 4. Art No.:CD009016. Doi: 10.1002/14651858. CD 009016.pub 2.) The authors rate the evidence as low to moderate and conclude that "forced air warming (FAW), applied in the surgical pre-or intraoperative phases or both, seems to have a beneficial effect in terms of a lower rate of surgical site infections and complications, at least in people undergoing abdominal surgery.."

In a response to concerns about safety, any increased risk of SSIs with forced air warming systems – the Bair Hugger, ECRI issued a report in 2013. After a critical review of the literature. The ECRI Institute, an independent review body with skills in evaluating data, found no sufficient evidence linking forced air warming to surgical site infections. (Health Devices April 2013 pp 122-125. www.ecri.org).

c. *Historical Cohort Studies*

Five historical studies have been reported to examine surgical site infections. These are important, "real-world" data to examine effectiveness of warming systems in actual practice. All five studies used forced air warming systems, and 4 of 5 warming systems were with the Bair Hugger. In one study, the rates of all infections, cardiac events, and mortality were also examined. Each asked the question, after the use of a forced air warming device, if patients avoided hypothermia, were the outcomes the same as or different from those who developed unwanted hypothermia? (See data in table below). A more recent 6th retrospective cohort study examined 4 different definitions of hypothermia to examine links to surgical site infections.

Study	Country, Device Reference	No. Patients and type if Surgery	Percent under 36^0 C	Outcomes (Risk Ratios) SSI / All Inf. / Morbid Cardiac Events	Mortality
1.	U.S. Warm Touch set @ 43^oC *Anesth* 2015; 123: 116-25	46,683 General Sgy	3%	.86 / .68* / .60* N.S. / *Significant, favoring warming Trend	.41*
2.	Holland **Bair Hugger** *J Arthroplasty* 2013; 28:895-9	THA* – 415 TKA *– 257	27%	Surgical Site Infections RR if cool 3.7 1% if warmed vs p=0.061 3.7% if hypothermic	
3.	Japan **Bair Hugger** set @ 38^o C *Surgical Infect* 2016 Doi: 10.10. 1089/Sur.2015. 182	1409 High risk GI patients. ~ half with cancer	37.5%	RR = 1.0 if severe hypothermia (<35^O C) Normothermia Mild Hypothermia	Infection rate 33.3% 19.2% 17%
4.	U.S. **Bair Hugger** Orthopedics 2016 39:e1170-77	1525 Orthopedic patients with hip fractures	17%	Multi-variable logistic regression for deep SSI: OR 3.30 (1.19 – 9.14) p=0.022	
5.	U.S. **Bair Hugger** Frisch NB et al Orthopedics 2017; 40:53-63	THA and TKA (N=2397)	44% 33%	1% if warmed 1% if not warmed	

* THA stand for total hip arthroplasty (replacement)
* TKA stands for total knee arthroplasty (replacement)

Inf = infections
N.S. = not significant

1. **The 2015 U.S. study at Hopkins showed a 3.7 – fold non-significant trend towards reducing SSIs but showed significant reductions of total infections, of morbid cardiac events, and deaths within 30 days.**

2. **The Dutch study of THA and TKA showed a benefit with warming at a borderline P value of 0.061. No clinician would ignore these beneficial findings in hip and knee arthroplasty patients.**

3. **The Japanese study showed no overall effect but an important reduction in patients with normothemia vs severe (<35°C) hypothermia in very ill patients.**

4. **The U.S. hip fracture study is the first and largest study analyzing the effect of intraoperative hypothermia in orthopedic patients. It showed a large protective effect if patients remained warm.**

5. **The U.S. study of THA and TKA showed no difference in warmed vs not warmed patients in terms of SSIs.**

In general, the studies show the benefits of warming. Four of the five used a Bair Hugger warming device, three studied orthopedic patients and two of the studies focused on patients with THA or TKA.

Very recently, Rebeccah Baucom and colleagues in a 6th retrospective cohort study used 4 different definitions of hypothermia to examine any link of hypothermia to SSI: temperature nadir, mean intraoperative temperature, percentage of time at the temperature nadir and percentage of time with a temperature of less than 36°C. The adjusted odds ratio, respectively, for the 4 metrics of hypothermia were 0.96 (.75-1.22). 1.10 (0.60 – 2:00); 1.02 (0.90 – 1.16) and 1.17 (0.76 – 1. 1.81). Thus, very small non-significant odds ratios linking infection to hypothermia were noted for 3 of the 4 definitions of hypothermia. (R.B. Baucom et al., Association of Perioperative Hypothermia during Colectomy with Surgical Site Infection. JAMA Surg 2015; 150: 570-5).

It has now been shown that pre-operative warming of surgical patients plus intraoperative warming has benefit over intraoperative warming alone. (Andrzejowski J et al., Effects of prewarming on post-induction core temperature and the incidence of inadvertent perioperative hypothermia in patients undergoing general anesthesia. Brit J Anaesth 2008; 101:627-51). In a study of 68 patients undergoing spinal surgery, 31 were prewarmed, and 37 controls were without prewarming. Both groups had operative warming with the Bair Hugger. A smaller decease in mean core temperature was noted in the prewarmed group at 40, 60 and 80 minutes after induction ($p<0.05$). The AUC (area under the curve) of the prewarmed group was greater during the procedures than the controls ($p<0.005$). Any comparison of warming systems should take into account the concurrent use of prewarming systems.

d. *Case Control Study*

Recently Brown and colleagues from the Mayo Clinic reported data from a retrospective case control study examining the relationship of SSI to intraoperative hypothermia in patients undergoing clean surgery. The 10 year study involved 1335 patients with a SSI and 3683 controls. The authors examined the relationship of SSIs with composite SCIP – 10 compliance [surgical care improvement project that seeks a goal of normothermia] (AOR 0.89; CI_{95} . 63 – 1.24); with temperature compliance (≥ 36° C) (AOR .92: CI_{95} .78 – 1.09); and forced air warming device documented (AOR.95: CI_{95} .76 - 1.19). None of the studies showed harm in the overall analyses. All adjusted odds ratios (AOR) were less than 1.0, suggesting a trend for fewer SSIs with warming compliance. None were statistically significant.

In further subset analyses (in their Table 4), there appeared to be a higher risk for SSI in general surgery patients, reduced risk in Neurosurgery patients, and trends for lower SSI rates if SCIP – 10 compliance was met for orthopedics, spine and vascular surgery patients. (Brown MJ et al. Intraoperative hypothermia and surgical site infections in patients with class 1/clean wounds: A case control study. J Am Coll Surg. doi: 10.1016/J. JAM Coll Surg. 2016. 10.050). It is of interest that the Mayo Clinic continues to use the Bair Hugger for surgery.

It should be noted that the Brown study (2016) was 20 years after the Kurz study (1996), 15 years after the Melling study (2001), and six years after the Darouiche study (2010) showing 40% reduction in SSIs with a switch from povidone-iodine to chlorhexidine alcohol skin preps.

It is likely that with increasingly successful efforts over time at controlling the microbiome and other risk factors for SSI, the residual modifiable factors were reduced, and study power to show a significant difference was low. The authors agree: "It is possible that these other measures at reducing SSI obscured any effect of perioperative hypothermia avoidance."

In summary, the benefits of warming are established and linked to reduced risk of SSIs. The Bair Hugger is established as an effective method of maintaining normothermia.

e. *National data in the U.S. in the era of the Bair Hugger.*

Trends in In-Hospital Major Morbidity and Infections after Total
Joint Arthroplasty: United States 1998-2008 – The increasing trends of comorbidity in U.S. patients. The manuscript by Kirksey et al *Anesth Anal* 2012; 115: 321-7 showed the following:

i. *The need to correct for rising comorbidities in the U.S.*

During the 1998-2008 study period, the number of total knee and total hip arthroplasties performed in the U.S. increased linearly (144% for TKA and 79% for THA); and by 2008, there were 616,000 TKA and 277,400 THA – thus twice as many knee as hip operations. Importantly, **the comorbidity burden (burden of underlying diseases) increased significantly over the study period** and was associated with postoperative complications including sepsis. Specifically, the comorbidity burden increased 35% for TKA and 30% for THA patients over the decade. The incidence density of sepsis after THA increased from approximately 2 to 2.5 per

1000 hospital days over the decade. Of note, increases in sepsis were linked to increases in the comorbidy index. The term "sepsis" is not equivalent to prosthetic joint infections and includes pneumonia, urinary tract infection, bloodstream infection, sinusitis and other infections.
The authors concluded that **"the number of THAs and TKAs performed in the United States is rapidly increasing in an increasingly comorbidity – ridden population."**

ii. *National Data Corrected for Comorbidities*
The data by Kirksey et al were confirmed in an analysis of the Mayo Clinic Total Joint Registry (1993-2005) known to have similar characteristics to the national U.S. cohort – see Sing JA and Lewallen D.G. Increasing Obesity and Comorbidity in Patients Undergoing Primary Total Hip Arthroplasty in the U.S.: A 13 year study of time trends. BMC Musculoskeletal Disorders 2014; 15:441. doi: 10.1186/1471 – 2474-15-441.

In multivariate analyses, compared to 1993-5, significantly more patients in 2003-5 had BMI $\geq$ 40 (OR 2.79 – CI_{95} 1.85 – 4.22); Deyo – Charlson comorbidity index $\geq$ 3 (OR 1.32; CI_{95} 1.07 – 1.63); depression (OR 2.25 – CI_{95} 1.66 – 3.05); and anxiety (OR 1.71 – CI_{95} 1.19 – 2.15). Thus, the odds of being morbidly obese or having many comorbidities were ~ 3 fold more common in 2003 – 5 vs 1993 – 5; and the odds of being depressed or having anxiety were ~ 2 fold more common in 2003 – 5 among joint replacement patients.
The authors concluded that **"studies of THA outcomes should take these rapidly changing patient characters into account."**

iii. *Corroborating Data on Comorbidity Rises in the U.S.*
In 1990, obese adults comprised less than 15% of the population in the U.S. states. By 2010, 36 states had obesity rates of $\geq$ 25%, and 12 of the 36 states had rates of $\geq$30%. **Current data show that 36% of U.S. adults are obese.**
CDC. Overweight and Obesity: Adult obesity facts
Flegal KM et al. Prevalence of obesity and trends in the distribution of body mass index among U.S. adults, 1999 – 2010. *JAMA* 2012; 307: 491-7.

The prevalence of diabetes mellitus (DM) has been increasing all over the world. A 2011 CDC report estimated that DM affected ~ 25.8 million people in the U.S. (7.8% of the population) in 2010, of which 90 – 95% are type 2. Obesity contributed to ~ 55% of cases of diabetes mellitus. Dept HHS. CDC, 2010. National diabetes fact sheet: National estimates and general information on diabetes and prediabetes in the U.S. http://www.cdc.gov/diabetes/pubs/pdf/ndfs - 2011.pdf. (Prevalence of overweight and obesity among adults with diagnosed diabetes United States, 1984-1994 and 1999-2000. CDC (November 2004) mmwr.mmwr; 5 (45): 1066 – 1068).

A more recent study shows that the trends for physician diagnosed diabetes mellitus in the U.S. rose from ~ 5% to 12% between 1988-94 and 2005 – 2010. (Mozaffarian D et al, Heart Disease and Stroke Statistics – 2016 Update, A Report From the American Heart Association, *Circulation* 2015; 131: e29 – e322.)

In addition to an increased rate of carriage of *S. aureus* in obese surgical patients, another factor linking obesity to elevated SSI risk is subcutaneous tissue penetration of perioperative antibiotics. The pharmacokinetics and tissue penetration of cefoxitin in obesity has been studied by Toma, et al. and colleagues (See Toma et al., Pharmacokinetics and Tissue Penetration of Cefoxiting in Obesity: Implications for Risk of Surgical Site Infection, *Anesthesia & Analgesia*, 2011; 113:730-7).

Obese patients (N=14) were given 2 Grams of Cefoxitin preoperatively and subcutaneous levels were compared to healthy volunteers (N=11) and nonobese patients (N=2). Subcutaneous tissue concentrations were similar in the normal – weight healthy volunteers given only 1 Gram of Cefoxitin and the normal weight patients. In contrast, the subcutaneous concentrations in obese patients given 2 Grams of Cefoxitin were lower than those in the normal – weight subjects receiving 1 Gram and were approximately half those of the normal-weight subjects.

Since approximately 68 % of American adults are overweight (BMI ≥25 Kg/M^2), 33% are obese (BMI > 30) and 6% obese (BMI ≥30) and 6% morbidly obese (BMI ≥ 40), the risk factor of obesity for SSI is a huge problem among patients undergoing surgery (Flegal et al., Prevalence and Trends in Obesity Among US Adults, 199-2008 JAMA 2010; 303: 235-41).

The point about comorbidities, e.g. obesity and diabetes, is that they increase the risk of a surgical site infection. Thus, crude rates may be expected to increase over time if comorbidity frequency increases. To maintain a level playing field and look at true changes over time, the effect of the comorbidities needs to be considered. By analogy to the financial world, to examine the value of a dollar over time, one has to correct for inflation over that period.

iv. Revisions of THA Over Time

The manuscripts by Kurtz et al. and by Cram et al. show the following:

- From 1990 to 2002 the number of revision procedures almost doubled for hip surgeries [tripled for knee surgeries]. (See Kurtz et al., Prevalence of Primary and Revision Total Hip and Knee Arthroplasty in the United States From 1990 Through 2002, *J. Bone Joint Surg Am.,* 87:1487-97, 2005)
- Revisions for total hip replacements constitutes ~ 20% of the volume of primary total hip replacements. (See Cram et al., Total Knee Arthroplasty Volume, Utilization, and Outcomes Among Medicare Beneficiaries, 1991-2010, *JAMA* 2012; 308:1227-36).

Infection rates are higher after revisions than for primary THA or TKA. Thus, when examining trends in infection rates, it is also important to separate the THA primary procedures and TKA primary procedures from combined THA and TKA data that also include revisions.

v. Notes on THA-Associated Infections and Sales of Bair Hugger Devices: United States

- Over time the number of THA and TKA and revisions increased.
- The increases in orthopedic operations for these procedures occurred in an increasingly comorbid patient population.
- Increases in sepsis over time were linked to increased comorbidity over time.

- Bair Hugger sales increased over time as hospitals chose to use the device for the increasing number of patients having surgery for THA and TKA and revisions of both.
- National data on THA show that between 1998 and 2008, infection rates increased from 2 to 2.5/1000 patient days.
- Increases in infection rates are correlated with increases in underlying comorbidity burden. At the NIS website the authors state that over time there is more bias likely in the earlier periods than more recent periods. Such statements suggest under reporting of infection rates earlier than later. Such underreporting earlier would tend to show a spurious rise in infections (sepsis) over time.
- **No national data support causal link of Bair Hugger sales to infections after THA or TKA.**

vi. *National Data Corrected for Comorbidities*

In 2013, a group of orthopedic surgeons examined the question, has the rate of in-hospital infections after total joint arthroplasty decreased? (Rasouli, et al., Has the Rate of In-hospital Infections After Total Joint Arthroplasty Decreased?, Clin Orthop Relat Res (2013) 471: 3102-11). They examined the National Inpatient Sample (NIS) database from 2002 – 2010. The numbers of primary THA increased from 200,000 to just over 300,000 during the study period.

In examining the rates of prosthetic joint SSI over time, they used a measure of comorbidity (the Elixhauser Comorbidities) to correct for underlying illnesses. The overall rate of SSI during the period was 0.31%. UTI and SSI rates were both relatively flat over the period queried, but multivariate analysis indicates that **when other demographic and clinical factors were controlled for, both infection rates dropped over time. This appears to be the first use of a comorbidity index to correct for confounders known to increase the risk of a surgical site infection after joint arthroplasty.**

Thus, substantial rises in comorbidities have been reported by Kirksey et al, confirmed by Mayo Clinic data, and noted in U.S. trends for obesity and diabetes mellitus in several studies. When comorbidity is controlled – leveling the playing field over time – it has been reported that surgical site infection rates have fallen over time during the use of the Bair Hugger.

- More recently the Centers for Disease Control and Prevention released their national data. (See CDC National and State Healthcare Associated Infections Progress Report, Based on 2013 Data, Published January 2015). **In the report they utilized risk adjustment models to correct for procedure related risk factors.** For THA and for TKA, comparing 2013 to a 2008 baseline, they show a **27% reduction in surgical site infections over time for THA and a 40% reduction over time for TKA. These data confirm the data of Rasouli et al. in showing reduced trending rates of SSI after joint arthroplasty in the era of the Bair Hugger.**

So far, two favorable clinical trials data, the combined studies' estimates from a meta analysis data, six historical cohort studies, a case-control study, and the national trends of infection rates after primary THA and TKA corrected for comorbidities show no harm with forced air warming and the Bair Hugger specifically. They often show remarkable benefit.

f. Available microbiological data that show no signal for a link to SSIs from the Bair Hugger and provide biological plausibility for its non-risk.

Clinical studies surely have more weight than laboratory and other non-clinical studies for examining cause and effect relationships. Nevertheless, if any harm from the use of the Bair Hugger could be likely, one might expect to see suggestions from bacterial studies in a real or simulated operating room. On the other hand, if bacteriological studies showed no likely risk, they would in fact be further support for the favorable and more relevant clinical data.

Between 1991 and 2013 there have been eight studies attempting to determine if the Bair Hugger system increases viable bacteria at the surgical site or in the air of the operating room

Author/Ref	Key Design Points	Outcome
R.S.Zink et al Anesthesia and Analgesia 1993;76: 50-53	8 volunteers on an OR table Agar plates placed on abdomen for 4 hours: 2h with warmer and 2h with control	No difference in CFU noted on the Agar culture plates
A.C. Hall et al Poster Dec 9, 1991 Postgrad Assembly in *Anesthesia* (PGA) NY, NY	20 patients undergoing maxillofacial surgery randomized to: Bair Hugger (BH) or no Bair Hugger; culture plates in OR	BH: 7.35 CFU mean/ plate No BH: 7.27 CFU mean/plate
J.K. Huang et al *Crit Care* 2003; 7.3: R 13	Air samples and wound specimens during 16 vascular surgery procedures using the Bair Hugger	A decrease in bacterial counts in air and around the patient after the use of the Bair Hugger
W.E. Dirkes et al *Anesthesiol* 1994 81: No 3A (Sept)	An agar plate of β-streptococci placed 10" from filter inlet; 2 warm air and 1 Bair Hugger. Air samples cultured.	No transmission in the air occurred of the streptococci during use of the Bair Hugger
B. Moretti et al *J Hospital Infect* 2009; 73: 58-63	Air samples during 30 THA (mean age 64 for patients); 3 different sampling sites. CFU counted/M^{-3}; means are illustrated	Empty Theatre: Site Mean CFU A1 17.8 A2 19.4 A3 19.2 Immediately after patient on table – before use: Site Mean CFU A1 79.2 A2 61.2

		A3 69.3 After Bair Hugger Site Mean CFU A1 41.7 A2 42.2 A3 42.2
M.S. Avidan et al *Anesthesia* 1997; 52: 1073-6	Experimental design in an empty OR; 9 Bair Huggers and 1 warm touch all convection warmers'; examine growth on agar plates	4/10 had growth if plates were directly in air steam 16" below the end of the hose. No growth, however, if warmers connected and blown through perforated blankets
L. Occhipinti et al Canad Vet J 2013; 54: 1157-9	Randomized study involving 100 canine surgeries; bacterial counts on surgical drapes counted before and after surgery	4/58 positive drapes afer Bair Hugger and 2/40 controls – no difference -
N. Tumia et al *J Hosp Infect* 2002; 52: 171 - 4	Air samples in 2 empty theatres and during 4 orthopedic operations (3 THA and 1 shoulder op.)	Non-significant rise in colony forming units (CFU) between empty theatre and warmer off and then a non-significant rise in CFU between warmer on and warmer off

In eight studies, 4 involved real patients, 1 was a veterinary study, and 3 involved simulated patients. **All the studies were small and overshadowed in causal inference by the clinical data reported above. Nevertheless, all microbiological outcomes showed no signal for risk vs controls.**

It should be noted that these publications between 1993 and 2013 were open and available to the public. These data stand in contrast to the unpublished, hidden data by Albrecht and others showing no increase in CFUs in various experiments with the Bair Hugger (see section vii b on particles, air bubbles, filter efficiency and cultures of the Bair Hugger apparatus). The unpublished data are further confirmation of the safety of the Bair Hugger.

More recently published data support the safety of the Bair Hugger (Oguz R et al. Airborne bacterial contamination during orthopedic surgery: A randomized controlled pilot trial: *J Clin Anesthesia* 2017; 38: 160-64). In that clinical trial 80 orthopedic patients were randomized to either forced air warming (Bair Hugger) or electric warming system (Hot Dog). The number of airborne bacteria was measured using sedimentation agar plates and nitrocellulose membranes at 6 standardized locations in the operating room. The authors report the following: In "multivariate analysis…the absence of unidirectional

turbulent free laminar airflow and longer duration of surgery increased bacterial counts significantly. The type of patient warming system and the number of health professionals had no significant influence on bacterial counts on any sampling site."

Summary – Benefits of avoiding hypothermia with use of forced air warming

Two clinical trials, one Meta-analysis, six historical cohort studies, one case control study, an independent review by the ECRI institute, two ecological national studies of prosthetic hip and knee infections in the Bair Hugger era, eight published microbiological studies, and seven unpublished and hidden microbiological studies of the Bair Hugger device are concordant with the conclusion that no harm results from use of forced air warming for surgical patients. A prospective clinical trial comparing the Bair Hugger vs the Hot Dog warming system showed no influence of either device on airborne colony forming units in the operating room. Almost all of the clinical studies employed the Bair Hugger warming system and several support a benefit, in fact, in reducing surgical site infections. No study shows harm with the Bair Hugger.

III. – Quality of the Data – Hierarchy in Ascribing Causal Relationships

In the hierarchy of studies designed to show evidence that one device is better than an alternative, prospective clinical trials are considered to have the highest quality and validity. These are prospective, controlled trials comparing one device to another in studies that are randomized and have blinded (masked) evaluation of critical end points. The studies have to be large enough to have an 80% statistical power to detect a clinically significant difference in the two systems if one exists. They are the gold standard for clinical decision making. If several small or large controlled clinical trials have been performed, a summary Meta-Analysis showing the average effect from all the data, can be performed.

In the absence of well-designed, large prospective clinical trials, large non randomized prospective cohorts showing a difference between one device vs another - examined concurrently - would be provocative and warrant a subsequent large clinical trial to show the relative value of the two systems being evaluated.

With respect to an alternative to the Bair Hugger, there has been no large prospective and controlled clinical trial showing a statistically significant improvement in outcome – a lower infection rate after surgery – with an alternative warming device.

There is no large controlled prospective cohort showing a statistically significant reduction in surgical site infection with use of an alternative to the Bair Hugger evaluated during the same study period.

There is also not a large retrospective trial - with concurrent use of both the Bair Hugger and HotDog device - suggesting a statistically significant reduction in surgical site infections with the use of an alternative to the Bair Hugger.

A single retrospective case-control study with many flaws suggested a better outcome with the Hot dog device than the Bair Hugger. The two devices were not compared concurrently, case finding methods were not described and many variables were not controlled. Only a univariate analysis was performed, and thus, the odds ratio reported is not supporting an independent predictor of infection. Several biases were present. See section VII C – The McGovern study.

At this point there are no compelling clinical data to show superiority of an alternative to the Bair Hugger for reducing surgical site infections. Specifically, no properly conducted clinical trial has shown that infection rates are significantly reduced with an alternative to the Bair Hugger. Current data do not show that an alternative to the Bair Hugger is safer than the Bair Hugger.

At the same time there are no compelling data to show that the Bair Hugger causes harm.

Hierarchy of Studies Designed to Show Evidence of Superiority of One Device to Another

1. Meta – analysis of several well conducted, prospective clinical trials that were controlled, randomized, and blinded (masked).
2. Single well conducted prospective clinical trial that was controlled, randomized and blinded (masked).

3. Large, well-designed prospective observational cohort studies with concurrent use of both devices and well defined case definitions and case finding methods with analyses that control for confounding variables.
4. Large, well-designed retrospective observational cohort studies with concurrent use of both devices and well defined case definitions and case finding methods with analyses that control for confounding variables.
5. Case-control studies in which the groups are analyzed retrospectively for risk factors for a specific outcome.
6. Cross sectional survey in which cases and controls are examined at specific moment in time. Better case control studies of alternative therapies are those in which the alternative options were used during the same study period. This approach controls for changes in other variables, that would not be corrected in before vs after retrospective studies.
7. Case series – a collection of cases that share a common time period or therapy; there is no effort to have concurrent controls or analyze for confounding variables.
8. Case reports.
9. Expert opinion.

   (See Greenhalgh T., How to read a paper Getting your bearings (deciding what eth paper is about, BMJ 1997, 315: 243-6)

Note: If no clinical studies are available to provide evidence, animal studies may provide clues which could be examined subsequently in human studies. If clinical data and no animal data exist, exploratory in vitro and other laboratory-based studies may be used to test initial hypotheses. Such studies would necessarily prompt better studies in the hierarchy of high quality methods for ascribing causal relationships. The outcome of interest, of course, should be SSIs comparing the Bair Hugger with an alternative warming device.

See graphics related to the Bair Hugger on pages 19 and 20 (Figures 2a – 2d).

2a. Hierarchy of Bair Hugger System Studies

Hierarchy of Bair Hugger System Studies

Clinical Studies: Gold Standard for Medical Research
Randomized studies examining impact of Bair Hugger system on rate of surgical site infections

Biological Plausibility Studies: Next best evidence
Studies of biologically plausible endpoints closely related to surgical site infections:

- Deposition of bacteria on wound site itself
- Movement of airborne bacteria

Exploratory Studies: lack clinical relevance and have no predictive value
Preliminary studies generally used to develop hypotheses for use in developing higher level studies

- Surrogate endpoints not correlated with surgical site infections, but inform whether biological plausibility studies are warranted
  - Movement of particles
  - Impact on airflow, non-mobilized bacteria
  - Heat differentials

31-01

2b. Clinical Studies

Clinical Studies

Clinical Studies explore impact of Bair Hugger system on surgical site infections

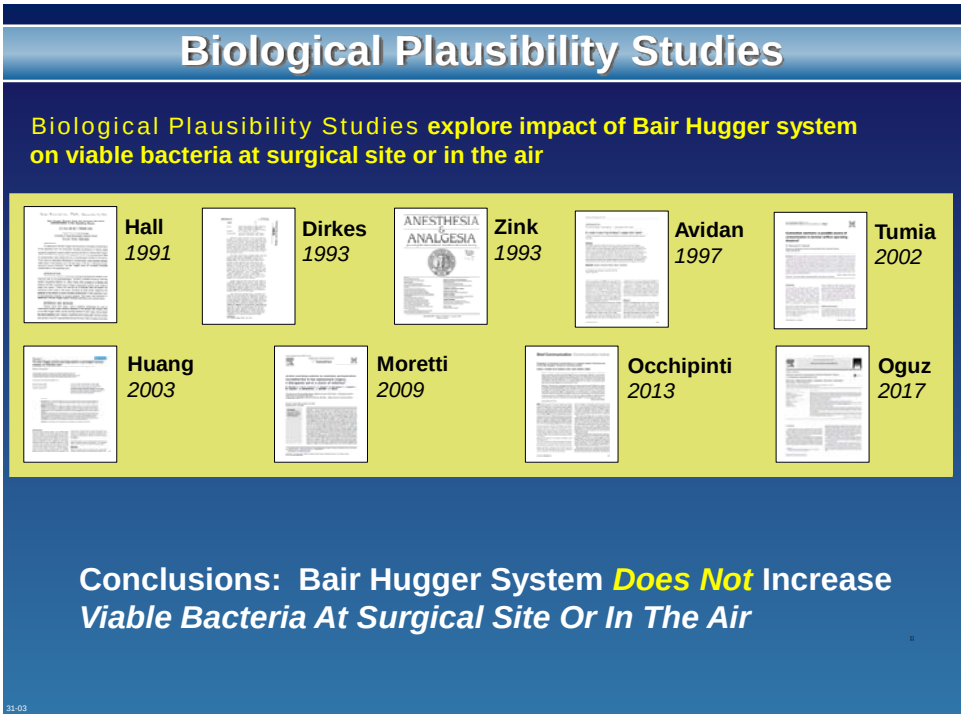
Kurz
1996

Melling
2001

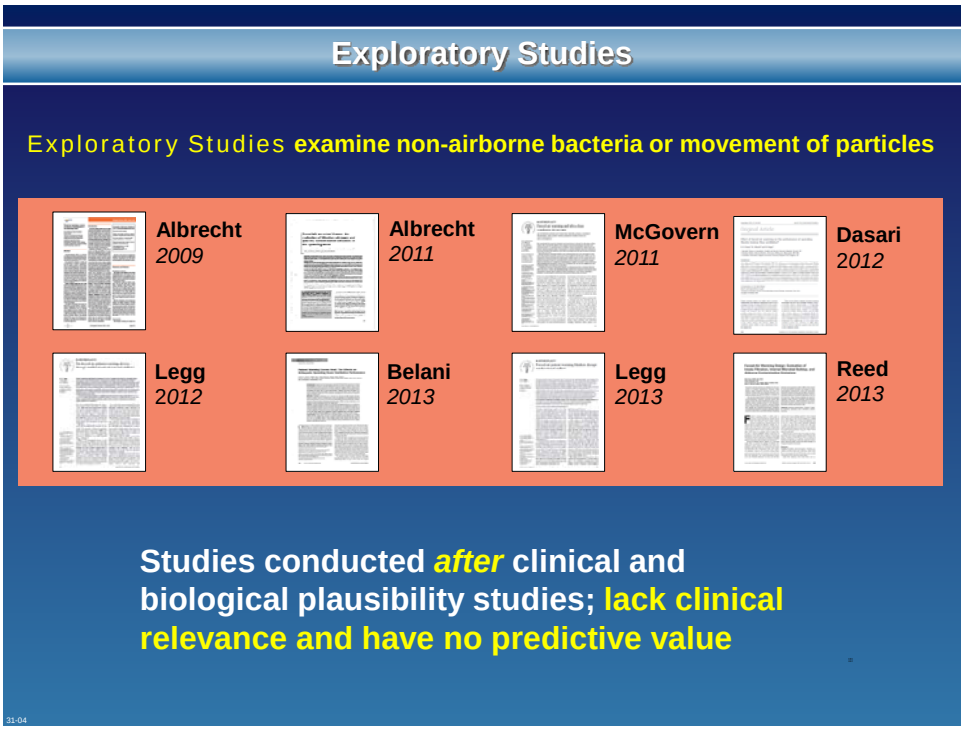
Conclusions: Bair Hugger System *Reduces* Surgical Site Infections

31-02

2c. Biological Plausibility Studies



2d. Exploratory Studies



IV. The Microbiome

Introduction: Infection is a multifactorial event with several contributing aspects to the risk. For any given mode of transmission (direct contact, fecal-oral, airborne, blood borne, large droplet and others), the infectious risk is influenced by the following:

- Organism exposure dose and inherent virulence
- Environmental risk factors
- Host factors

In surgical site infections, host factors are very important. These include the participants' own comorbidity risk factors, genetics, immune status, and the microbiome of the patient. Below I introduce the concept of the host microbiome as part of host defense against infections.

a) Role of the Microbiome

The term microbiota is commonly used to describe the community of microorganisms (bacteria, yeasts, viruses) that colonize our skin, nasal passages, throat, vagina and gastrointestinal tract. The term *microbiome* is used to define the total aggregate of microbial genes located at a specific part of a person's body. I will use the term microbiome for both. Since many species of the microbiome cannot be cultured using standard methods, investigators have used new techniques to identify microbial genes to study the microbiome. A healthy microbiome assists people in warding off the very offensive bacteria e.g. strep or staph that can cause serious infections. People and various microorganisms colonizing the human body live in a "peaceful coexistence" relationship if we remain healthy. If the numbers of some bacteria become very large, if the bacterial composition of the microbiome is altered, or if the person's immune system fails, however, infection can occur.

Not surprisingly, antibiotics can sometimes kill off some of the "good" bacteria and allow a harmful one to dominate and cause infection. An example of the latter is the appearance of *Clostridium difficile* colitis, a serious and sometimes life-threatening infection of the colon after antibiotic use. The antibiotics kill off the "good" flora of the intestine, cause major alteration in bacterial composition, and select for the overgrowth of the *Clostridium difficile*. What is striking is the almost complete reversal of the infection in days after restoration of normal flora. (See S. Khanna et al, A Novel Microbiome Therapeutic Increases Gut Microbial Diversity and Prevents Recurrent Clostridium difficile Infection, *J. Infect Dis* 2016; 214: 173-81; Vehreschildet al., Fecal Microbiota Transfer 2.0, *J Infect Dis 2016;* 214: 169-70).

b) Numbers of bacteria of the microbiome

A perspective on the importance of the microbiome relates to numbers: on our body we have 10^{13} human cells (a 1 followed by 13 zeros). However, on our skin and mucous membranes we have 10^{14} microorganisms – thus 10 times as many microbes as human cells! When one examines the aggregate of microbial genes, they outnumber human genes by a factor of 1000 (EA Grice, The skin microbiome: potential for novel diagnostic and the therapeutic approaches to cutaneous disease, *Semin Cutan Med Surg 2014*; 33: 98-103). It is now recognized that the community of microbes and their genes can influence the outcome of the interaction of people and microbes. The same genus and species can cause serious infections in some patients and become "neutral," colonizing bacteria in others.

On the skin, each of the bacteria, yeast, and virus family members of the microbiome has a preferred location on the body, depending on local moisture or distribution of sebaceous glands or hair follicles, etc. Thus, certain organisms dominate some sites on the body and other organisms on other parts. If we injure our skin, an infection may result and is often due to the organisms living nearby on that part of the skin.

In people, maintaining a protective community of usual microbes on the body is important for health.

c) The role of the microbiome and surgical site infections

Without the protection of the skin barrier nearby, organisms that are part of the skin microbiome can invade the deeper layers of the skin and soft tissue below. In surgery, the integrity of the skin is disturbed by the incision, posing a risk of infection: organisms living in harmony in the nose, throat or skin near the incision can find their way to the incision site and cause a surgical site infection (SSI).

A cross-section of the skin (figure 3) shows the top layers of the epidermis and dermis, below which lies the subcutaneous fat tissue and then the muscle and bone tissues. Piercing the dermis are the tubules from the sweat glands and hair follicles of the sebaceous glands, located in the subcutaneous tissue. [Figure 4].

The sweat glands help regulate temperature, and the sebaceous glands provide sebum which lubricates the top layers of skin and provides a water proof surface.

Figure 3

Importantly, bacteria of the microbiome reside not only on the skin surface but also on the hair follicles and in both the sweat glands and sebaceous glands (figure 4).

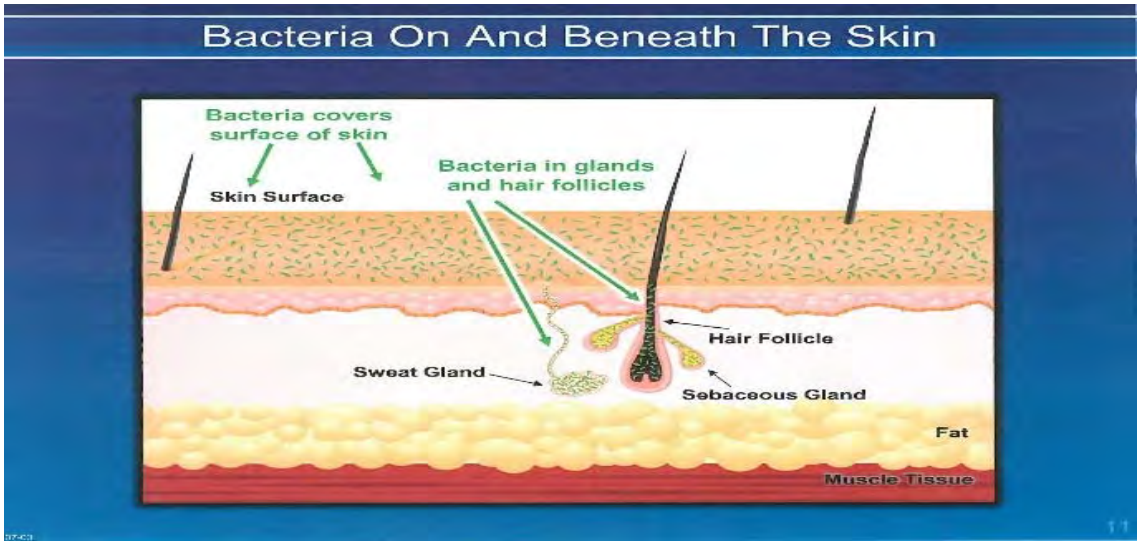


Figure 4

At the time of surgery the skin near the incision is prepped with an antiseptic designed to reduce the numbers of bacteria there. However, no current skin prep will kill all the bacteria on the surface nor the organisms below the surface in the sweat glands or sebaceous glands.

One can now see that if we could control the microbiome, we might prevent SSIs. Specifically for clean surgery, if we can control the microbiome of the skin and nasal passages, we will reduce the rate of SSI. Conversely, if we fail to control the microbiome, a surgical patient will develop a surgical site infection. Prior to surgery we physicians attempt to control the patient's microbiome by suggesting chlorhexidine showers to reduce the burden of staphylococcus and other bacterial counts on the skin; topical nasal antibacterial creams to "decolonize" the nose of *Staphylococcus aureus*; and best skin antiseptic preps just before the incision. To reduce the burden of infectious organisms in general, intravenous antibiotics are administered preoperatively to achieve a high blood and subcutaneous tissue concentration at the time of the incision.

Some patients are at higher risk than others for getting a surgical site infection by virtue of their having some underlying conditions such as diabetes mellitus, older age, obesity and other "comorbidities." It is thought that these conditions in some way alter the body's immune system or change the composition or nature of the microbiome.

Changes in the microbiome of the intestine have been noted in the following conditions: Obesity, diabetes mellitus, celiac disease, and others.

I am unaware of definitive studies to examine the skin microbiome in all of these conditions. However, an early study of *S. aureus* nasal carriage in children and in adults showed higher carrier rates in diabetics: See Smith JA et al, Basal Carriage of Staphylococcus aureus in Diabetes Mellitus, Lancet 1966 pp 776-7.

Children (157/531 were diabetic)

S. aureus Carriage:

Diabetics 76%

Non-Diabetics 44%

Adults (324/578 were diabetic)

S. aureus Carriage:

Insulin Dependent Diabetics 53%

Non-Insulin Dependent Diabetics – 35%

Non-Diabetic 34%

In 2008, Gorwitz RJ et al reported on the changes in the prevalence of nasal colonization with S*taphylococcus aureus* in the United States, 2001 – 2004. In the NHANES survey they found that **colonization with MRSA was independently associated** with healthcare exposure in males, with U.S. born, age >16, **diabetes**, and poverty in females. (Gorwitz et al., Changes in the Prevalence of Nasal Colonization with Staphylococcus aureus in the United States, 2001-2004, J Infect Dis 2008; 197: 1226-34).

A 2006 study of *S. aureus* carriage in diabetics and non-diabetics in Japan showed that independent risk factors for carriage were insulin use (OR 3.32) and antibiotic usage within the prior six months (OR 5.750). (See, Tamer et al., Staphylococcus aureus in Nasal Carriage and Associated Factors in Type 2 Diabetic Patients, Jpn. J. Infect Dis. 2006; 59: 10-14).

In a study of 137 cases of community – associated MRSA (CA MRSA) cellulitis, the independent risk factors for MRSA vs other causes of cellulitis - included obesity (AOR 2.33 – CI_{95} and the presence of abscesses (AOR 2.72 - CI_{95} 1.27 – 5.83). (See Khawacharoenporn, et al., Risk Factors for Community – associated Methicillin-resistant Staphylococcus Aureus Cellulitis – and the Value of Recognition, Hawai Med J, 2010; 69: 232-6)

In a study of obesity and *Staphylococcus aureus* nasal colonization among 2169 women and 1709 men in a general population, Olsen and colleagues found that in women**, each 2.5 kg/M^2 increase in BMI was associated with a 7% higher odds of *S. aureus* nasal colonization (p=0.01).** BMI was not associated with *S. aureus* nasal colonization in men, but high waist circumference was linked in men to *S. aureus* nasal carriage.

See Olsen K et al, Obesity and Staphylococcus *aureus* nasal colonization among women and men in a general population. P105ONE 2013: 8(5); e 63716. doi: 10. 1371/journal.pone.0063716.

Herwaldt LA et al described preoperative risk factors for nasal carriage of *Staphylococcus aureus*. Of 4030 patients, 891 (22%) carried *S. aureus.* **Independent risk factors for *S. aureus* nasal carriage included obesity (OR 1.29 with CI_{95} 1.11-1.50);** male gender (OR 1.29 with CI_{95}) 1.11 – 1.51); and a history of cerebrovascular accident (OR 1.53 with CI_{95} 1.03 – 2.25). (Herwaldt et al, Preoperative Risk Factors for Nasal Carriage of Staphylococcus aureus, Infect Control Hosp Epidemiol 2004; 2: 481-4.)

With respect to the microbiome one can say that certain conditions alter the composition such that diabetes and obesity increase nasal carriage of *S. aureus*. Nasal carriage of *S. aureus* is inked to increased risk of *S. aureus* SSI. Both diabetes mellitis and obesity are linked to increased risk of SSI, and some portion of that risk can be accounted for by the altered microbiome of the nasal passages.

Recently two microbiologists suggested that we abandon the term "pathogen' and instead focus on the reaction that occurs when a microbe interacts with a person. That interaction, described by Casadevall and Pirofski, yields one of three possibilities: infection (damage occurs); colonization (indifference) or commensal (benefit). These authors now incorporate the microbiome into the model, implying that variations in a person's microbiome influence the host response to a microbial challenge. Thus, a person and her microbiome are inseparable. (Casadevall and Pirofski, Ditch the term pathogen: disease is as much about the host as it is the infectious agent-the focus on microbes is hindering research into treatment, Nature 2014; 516:165-7.)

Interim Summary

We can think of the microbiome as part of the body's immune defense system. So in simple terms, if in any way we alter the microbiome defense system, the risk of infection rises. Both the density of the organisms and the composition are important factors.

When a patient requires surgery, it is important to assess that individual's risk for infection: What are the underlying illnesses that might alter the microbiome and increase risk? Has the patient been on antibiotics in the past 6 months that might have altered the composition of the microbiome? Are there several underlying problems such as obesity or diabetes that might combine to alter the microbiome and add risk for a surgical site infection? Afterwards we might ask, if a patient acquires a SSI, what is the likely origin of the offending organism causing the infection, and could it have become a preoperative member of the microbiome? Were all opportunities to reduce the risk of a SSI met with a good response?

d) Skin microbiome as the key source for SSIs after clean surgery

In 2010, Rabih Darouiche and colleagues reported a study comparing two alternative skin preps for reducing SSIs. In a study at 6 hospitals, 849 patients were randomized to receive the standard povidone iodine antisepsis vs chlorhexidine – alcohol skin prep. Within 30 days of surgery, infection occurred in 16.1% assigned to the standard povidone-iodine vs 9.5% assigned to the chlorhexidine – alcohol arm. **The use of a chlorhexidine-alcohol skin prep is linked to a 40% *incremental* reduction of all SSIs resulting from reducing the microbiome of the skin at the area of the incision. (Dariouche, et al., Clorhexidine-Alcohol versus Povidone-Iodine for Surgical Site Antisepsis, N Eng J Med 2010; 362: 18-26.)**

In another study, among 1147 patients undergoing a caesarian delivery those assigned randomly to chlorhexidine – alcohol prep had a relative risk of a SSI of 0.55 (Cl_{95} .30-.90), compared to these whose iodine-alcohol. **Thus, reducing the microbiome with a better prep reduced SSI by 45%.** This study again illustrates the critical role of the microbiome. (*New Engl J Med* 2010; 362:18-26. M.G. Tuuli et al., A Randomized trial comparing skin antiseptic agents at Cesarean delivery, N. Eng *J Med 2016*; 1-9)

The 40% reduction in surgical site infections after better controlling the microbiome of the skin with topical chlorhexidine alcohol is an incremental improvement – above that expected with povidone-iodine. Although there are no clinical trials of povidone – iodine vs placebo control in surgical patients, some insight into the value of povidone iodine can be gleaned from the study by A. Gravett et al. That team performed a prospective, randomized study of 500 consecutive patients entering the emergency room with traumatic lacerations requiring sutures. Half of the group had a wound irrigation with normal saline without scrubbing, and half had a 60 second wound irrigation and scrubbing with 1% povidone – iodine (Gravett et al., A trial of povidone-iodine in the prevention of infection in sutured lacerations, Ann Emerg Med 1987; 16: 167-71).

Of the 201 povidone – iodine wounds followed up, 11 became infected (5.4%) (2 became purulent). Of the 194 control wounds followed, 30 became infected (15.5%) $p< 0.01$(12 were purulent). **Thus, in that study ~ two-thirds of possible infections were eliminated with povidone – iodine and one-third remained.**

If similar data would apply to general surgery patients ie if povidone iodine was already preventing two-thirds of infections, then removing an incremental 40% on the remaining one-third with a switch to a chlorhexidine – alcohol prep would be an absolute removal of an additional 13% (40% times 1/3 residual). The absolute remaining proportion of wounds still not controlled with chlorhexidine – alcohol would be one-third (33%) minus 13% or 20%. This rough estimate based on clinical trials suggests that 80% of potential SSIs can be currently eliminated with control of the microbiota of the skin. Even if povidone-iodine reduced total infections by only one-third, the 40% reduction of the remaining two-thirds (27%) plus the 33% already controlled by povidone iodine would imply a 60% control currently with skin prep alone. (Figure 5).

(See Gravett et al. A trial of povidone – iodine in the prevention of infections in sutured lacerations. Ann Emerg Med 1987; 16: 167 – 71.)

Modeling Residual SSI Source with Increasing Efficacy of Skin Preps

If Iodine Reduces 2/3 SSI

1/3 (33%) SSI Residual

If Iodine Reduces 1/3 SSI

2/3 (67%) SSI Residual

Figure 5

Further reduction of residual by 40% with chlorhexidine – alcohol

33% - 13%

67% - 27 %

20% residual

80% SSI eliminated

20% Residual

60% SSI Eliminated

40% Residual

40% residual

e) Mapping the Microbiota of the Skin – A Marker organism, *Propionibacterium acnes*

In recent years it has become possible to begin to map the microbiome of the skin by looking at the genes of the bacterial microbiome at specific locations, a much more sensitive approach than cultures of organisms. Among the findings are that *S. aureus* is common to all areas of the skin but especially so in the under arm, groin, the webs of toes – areas of high humidity. Additionally, the upper back and upper chest is disproportionately colonized with

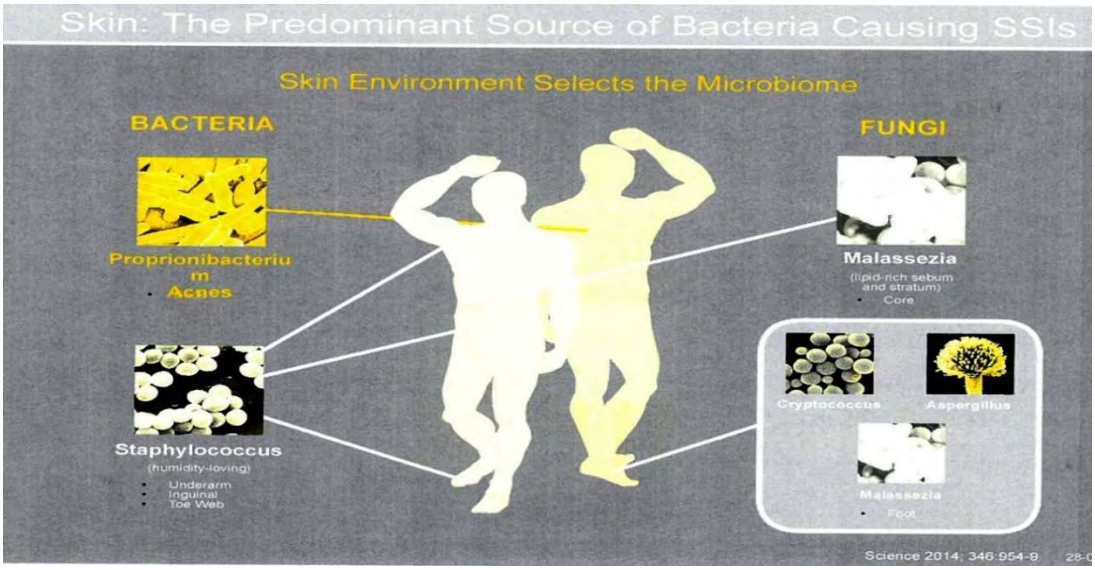


Figure 6

Propionibacterium acnes, an anaerobic, rod – shaped organism that prefers the environment of high levels of sebaceous glands. This species uses the sebum produced by sebaceous glands to grow and to metabolize to free fatty acids that help bind the organism to the upper back and upper chest. (Figure 6). If the local microbiome is the source of SSIs, one might expect that infection near the shoulder would show this marker organism more often than infections after knee or hip surgery that involve incisions over body surfaces not prevalent with sebaceous glands and *P. acnes.*

In that respect, it is of interest is to examine the bacterial causes of prosthetic joint infections (Figure 7). Whereas *S. aureus* and coagulase – negative staphylococci account for 43-83% of infections after joint implants, 24% of infections of shoulder joint prostheses are caused by *P. acnes*, the organism living near

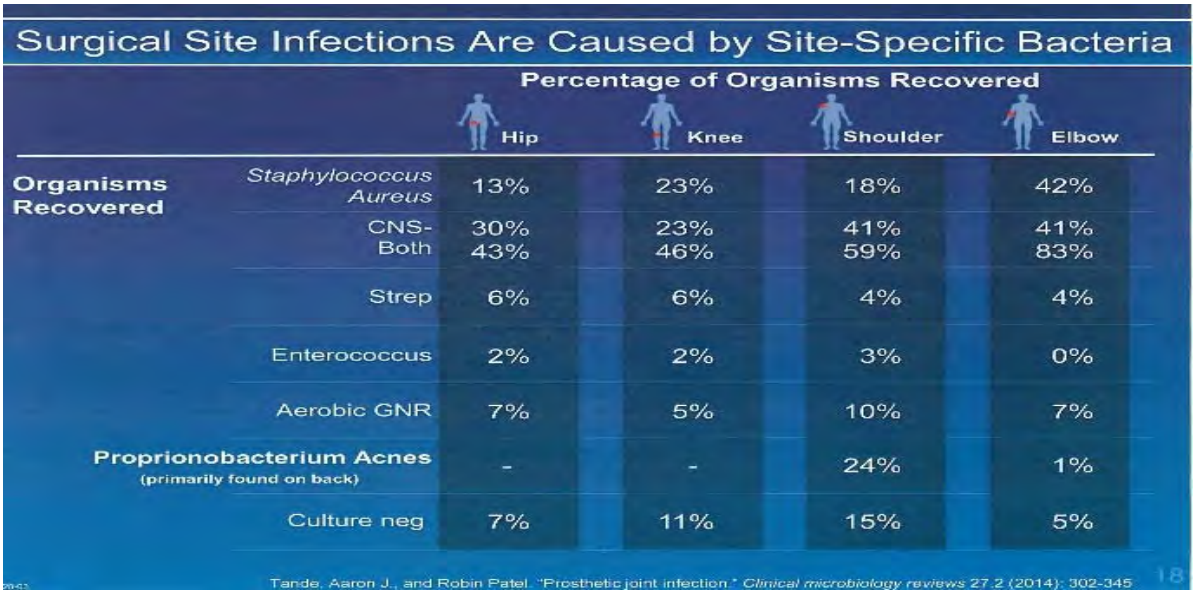


Figure 7

the incision site for that operation. It is commonly found in shoulder prosthetic joint infections. (See Tande A and Patel R., Prosthetic Joint Infection, *Clin Micro Rev* 2014; 27: 302-45). This is a useful organism to study SSIs, since it is a marker organism, one not ubiquitous as coagulase negative staphylococci.

Corroborating findings include the fact that up to 51% - 56% of infections after rotator cuff surgery of the shoulder are caused by *P. acnes*. *P. acnes* is <u>not found commonly</u> after joint surgery of hips or knees or elbows. (P.Y. Levy et al., Propionibacterium acnes Postoperative Shoulder Arthritis: An Emerging Clinical Entity, Clin. Infect Dis 2008; 46: 1884-6; G.S. Athwal et al., Deep infection after rotator cuff repair, J Shoulder Elbow Surg 2007; http:// dx.doi.org/10.1016/S. JSE 2006.05013).

In addition to the link of the microbiome near the shoulder and subsequent infections with *P. acnes* are also supportive microbiological data on similar patients with shoulder surgery:

- P.M. Sethi and colleagues examined the frequency of *P. acnes* found in 57 patients undergoing primary shoulder arthroscopy. Most patients (58%) were undergoing rotator cuff repair. Positive skin cultures for *P. acnes* were found in 8.8% of patients before the incision <u>and after the skin prep</u> but as high as 31.9% at closure. 56% of patients had at least 1 positive culture, and 22.8% had <u>≥</u> 3 positive cultures.

(Sethi et al., Presence of Propionibacterium acnes in arthroscopy: results of aspiration and tissue cultures, J Shoulder Elbow Surg 2015 796-803, http://dx doi.org/10.1016/j.jse.2014.09.042)

In the discussion the authors noted that Matsen et al found *P. acnes* in 76% of non-prepped skin and an intraoperative 55% rate of positive cultures for a dermal layer in another patient group. Similar to the data of Sethi et al, Saltzman et al found only a 7% rate of *P acnes* after chlorhexidine – alcohol skin prep. (See F.A. Matsen et al, Origin of Propionibacterium in Surgical Wounds and Evidence Based-Approach for Culturing Propionibacterium from Surgical Sites, J Bone Joint Surg Am 2013; 95 (23): @ 1811-7. http:// dx.doi. org/10.2106/JBJS. L. 01733)*M.D. Saltzman, et al, Efficacy of Surgical Preparation Solutions in Shoulder Surgery, J Bone Joint Surg Am 2009; 91: 1949-53. http://dx.doi.org/10.2106/JBJS.H. 00768.*

Thus, the organism is nearby, accounts for a significant proportion of infections seen, in both rotator cuff shoulder repair and infections after prosthetic shoulder replacement, and is apparently not well controlled with existing antiseptic preps. It is already present at the surgical site before the incision.

- Sethi's group followed up with a study of the efficacy of topical benzoyl peroxide on the reduction of *P. acnes* culture during shoulder surgery.
  (J.R. Sabetta et al., J Shoulder Elbow Surg. 2015, 995-1004; http://dx.doi. Org/10.1016/J.JSE. 2015. 04.003)

The authors recognized that *P. acnes* resides in the sebaceous glands, that chlorhexidine – alcohol prep was inadequate for eliminating the organism at the time of surgery, and that benzoyl peroxide (BPO) commonly used to treat acne, penetrates the pilosebaceous duct. They hypothesized that BPO would incrementally reduce the burden of *P. acnes* in addition to the skin prep with chlorhexidine-alcohol. 5% BPO was administered topically twice a day preoperatively and on the morning of surgery – 5 doses total.

50 patients were studied, and most (68%) were undergoing rotator off repair. Before the skin prep, 16% of the BP0 surgical site had *P. acnes* vs 32% on the skin of the deltoid on the untreated arm p=0.0001. The axilla was positive in 8% of BPO treated arms vs 28% of the untreated arms (.p=0.013).

After skin prep, with 3 applications of 2% chlorhexidine gluconate, 6.25% of samples grew *P. acnes* – a non-significant difference from control air swabs at 4%. At the end of surgery, 10% of skin cultures were positive, also not significant from air swab cultures.

The BPO application reduced pre-prep cultures by ~ 50% vs the control arm. **After adding the chlorhexidine alcohol prep, there was a further reduction of positive cultures for *P. acnes* from 16% on the deltoid to 6%, and from 32% in the axilla to 6% (See Table below):**

Rate of Positive *P. acnes* Cultures by Specimen

Control Air Swab 4% End of procedure : Axilla surgical side – 10% Skin anterior deltoid surg side – 10%	Skin anterior deltoid/Axilla Before preps: BPO side deltoid – 16% BPO side axilla – 8% No BPO side deltoid – 32% No BPO side axilla – 28% ↓ After skin prep ↓------ Ant deltoid surg side – 6% Axilla surg side – 6% Joint fluid – 4 % Tissue 1, 2,3-6%, 2%, 6%

The study confirms the dermis as the primary source of *P acnes;* BPO – a drug that penetrates the pilo-sebacious gland microbiome - reduced the risk of having a positive culture for *P acnes*, above a baseline and also above the rate seen after a skin prep. This drug has not been tested to measure its efficacy in reducing SSIs.

Currently, best estimates are that with improved skin preps the microbiome is better controlled and SSI rates have been reduced by 60-80%. With the marker organism, *P acnes*, proof of concept of the need to control the microbiome prior to shoulder surgery was shown with BPO, a drug that penetrates the pilo-sebacecus gland, affecting the microbiota.

- The skin adjacent to the spine is also a site for *P. acnes* residence. Among 489 patients operated on for correction of scoliosis studied by Richards and Emara, 23 developed delayed infection. *P. acnes* was positive in 12 (53%) of the 23 patients in the specimens obtained at the time of instrumentation removal (Richards, et al., Delayed Infections After Posterior TSRH Spinal Instrumentation for Idiopathic Scoliosis: Revisited, Spine 2001; 26: 1990-5). In another study, Sampedro and colleagues cultured the spinal implants of 22 patients with SSI and detected *P*

acnes in 9 (41%) of the 22 patients. (Sampedro, et al., A Biofilm Approach to Detect Bacteria on Removed Spinal Implants, Spine 2010; 35: 1218-24). In a third study, Shiono and colleagues sent specimens for culture during spine correction surgery for scoliosis (N=80): 1) Swabs of the skin after povidone – iodine prep but before draping; 2) laminae bone immediately after exposure; 3) laminae bone immediately after screw placement; 4) laminae bone immediately before wound closure; 5) bone fragment immediately after exposure and kept covered; and 6) a bone fragment immediately after exposure but kept uncovered.

No SSIs occurred. Positive cultures for bacteria were found in 1) 31%; 2) 25%; 3) 31%; 4) 33%; 5) (7.5%) and 6) 9%). *P. acnes* were recovered in 15 and *P. species* in another 9. Aerobic Gram positive cocci were found in 3 and other bacteria in 6 specimens (Shiono, et al, Sterility of Posterior Elements of the Spine in Posterior Correction Surgery, *Spine* 2012; 6: 523-6). These are further data supporting the concept that local flora at the site of the incision harbor the bacterial that cause a large proportion of SSIs. The study by Shiono et al shows also that organisms are present soon after skin prep and soon after incision. Brian Walcott and colleagues in a review of infections following operations on the central nervous systems states that "..bacteria penetrate the wound at the time of the initial surgical exposure. It is likely that most wound infections are the result of direct contamination with the local microbiome…" The subtitle of his article is "deconstructing the myth of the sterile field" (Walcott, et al., Infection following operations on the central nervous system; deconstructing the myth of the sterile field, *Neurosurg. Focus* 2012; 33: 1-9, DOI: 10.3171/2012.8.FOCUS12245). The implication is that surgeons do their best to minimize the number of bacteria at the incision site, but it is never sterile but as clean as possible, given the microbiome and human activity in disturbing the microbiome.

Corroborating support that the airborne route of infection is not common in surgery and that the patient's microbiome is the source comes from observational data of Tammelin and colleagues. They prospectively studied a cohort of 65 adults undergoing elective coronary artery bypass grafting – with or without concomitant value replacement. They focused on the source and route of transmission of methicillin – resistant *Staphylococcus epidermidis* (MRSE) in the surgical wound (Tammelin, et al, Source and route of methicillin-resistant Staphylococcus epidermis transmitted to the surgical wound during cardio-thoracic surgery. Possibility of preventing wound contamination by use of special scrub suits, *J Hosp Infect* 2001; 47: 266-76).

Pre-incision cultures of the sternum and legs (vein donor site), air cultures in the operating room, OR staff members' cultures of hands after the initial scrub, and wound cultures just before closing were examined. Patients with MRSE on sternal skin had a higher rate of MRSE in the wound than those with no MRSE on the sternal skin (RR = 2.429 CI_{95} 1.43-4.10). Recovery of MRSE in the air during operation or on the hands of the scrubbed team was not linked to finding MRSE in the wound. The significance of sternal skin as the source of MRSE wound contamination was supported by fingerprinting the organisms (pulse field gel electrophoresis): 3 of 4 traceable isolates originated from the sternal skin at the incision site. In the same study patients were divided into those whose surgical team wore conventional scrub suits with a fabric air permeability of 121.L/min vs those with a cotton and polyester weave mid an air permeability of only 2.5 L/min. No mention of randomization was made. The authors note that the reduction of total air counts of bacteria by use of the tightly woven scrub suits did not reduce the air counts of MRSE or wound contamination with MRSE.

f) *S. aureus* Carriage and Risk of a SSI

One of the most feared organisms in prosthetic wound infections, and very common is *S. aureus*. A key question is where did the *S. aureus* originate? Data from various studies indicate that the majority come from the patients themselves. Furthermore, controlling the microbiome of the nares with topical antibiotics is linked to a significant reduction in *S. aureus* SSIs.

In the pre- Bair Hugger era (1959 – 1969), it was shown that 33 to 100% of surgical patients in 8 different studies had *S. aureus* SSIs that matched the strains carried in their nares. (See review by Wenzel and Perl J *Hosp Infect* 1995; 31:13-24. – The following Table is from that review).

S. aureus surgical site infections and the proportion of endogenous sources

Rates of postoperative wound infection in nasal carriers and non-carriers of *Staphylococcus aureus*

Rates of wound infection

First author	Year of report	No. infected/ No. colonized	No infected/ No. not colonized	% Endogenous*
White	1964	20/106 (19%)	28/345 (8%)	66
Williams	1959	20/276 (7%)	7/342 (2%)	55
Public Health Laboratory	1960	73/821 (9%)	158/2235 (7%)	33
McNeill	1961	12/74 (16%)	11/113(10%)	42
Henderson	1961	22/264 (8%)	18/569 (3%)	30
Bassett	1963	24/442 (5%)	6/78 (8%)	58
Calia	1969	19/96 (17%)	16/173 (9%)	100

* By phage-typing-showing same strains in preoperative nasal culture as identified in postoperative wound infections.
In none of the studies was the pathway to infection studied among carriers.
From a review by Wenzel RP and Perl TM, The significance of nasal carriage of staphylococcus aureus and the incidence of post-operative wound infections.
J Hosp infect 1995; 31:13-24.

The data show the rates of *S. aureus* SSIs among surgical patients who were *S. aureus* carriers were 2 to 3 times greater among carriers than non-carriers. *The Bair Hugger had been in use for only 25 years in 2012; thus, none of these studies above were performed in the era of the

Bair Hugger. Thus, the carriage of *S. aureus* has been a recognized risk factor for *S. aureus* SSIs independent of forced air warmers.

Data from the review, shown in the table, illustrate the strong association of *S. aureus* SSIs and prior carriage of the same organism by patients undergoing surgery. The median data among studies showed that 55% of SSIs were endogenous strains carried pre-operatively (Williams). It is unclear how the patients acquired the infection, but they occurred without any warming device in use.

These data – well before the advent of the Bair Hugger – were confirmed in a 1963 report by J Burke from Harvard. In their quest to identify the sources of staphylococci contaminating the surgical wound during operation, they found that in 50% of operations studied (N=50), **"Strains of staphylococci found in the patients' nose, throat or skin in the region of the proposed surgical wound were also identified in the wound just prior to closing."** (John F. Burke, Identification of the Sources of Staphylococci Contaminating the Surgical Wound During Operation, Ann Surg 1963; 158:898-904).

In a study of the safety and efficacy of intranasal mupirocin for the elimination of *S. aureus* carriage, Reagan and colleagues showed the following (Reagan, et al. Elimination of coincident *Staphylococcus aureus* nasal and hand carriage with intranasal application of mupirocin calcium ointment, Ann Intern Med 1991; 15:101-6).

Among nasal carriers of *S. aureus*, 30-50% had the same organism on their hands pre-treatment, and elimination of nasal carriage was significantly linked to a reduced hand carriage after therapy: 2.9% in the treated group vs 57.6% in the controls. This 53% difference was significant, after adjustment for the baseline frequency of hand carriage.

This study shows that nasal carriage is a marker for *S. aureus* carriage elsewhere on the body, and elimination of nasal carriage is linked to elimination of non-nasal carriage.

L.A. Mermel and colleagues examined known carriers of MRSA (N=60) and examined nasal and extranasal colonization. Samples showed positive cultures of $\geq$ 1 site in 53 of the 60. Sensitivity for a positive culture was 91% for nares, 63% for groin, 47% for perineum and 32% for the axilla. A relationship was found for $\log_{10}$ counts in the nares and greater number of body sites colonized with MRSA. A correlation between diabetes and $\log_{10}$ counts in the perineum was shown. (L. A. Mermel et al. Methicillin – Resistant *Staphylococcus aureus* colonization at different body sites: A prospective quantitative analysis. J Clin Micro 2011; 49:1119-21).

Since nasal carriage predicts carriage of *S. aureus* in the groin and perineum, it is reasonable to postulate that failure to control the carriage in the nose leads to failure to control the microbiome of the groin and perineum.

A number of more recent studies show similar results to those in the pre-Bair Hugger era. In a follow up randomized clinical trial among surgical patients, in the subset with nasal carriage of

S. aureus, 4 percent of those who received preoperative nasal mupirocin had nosocomial *S. aureus* infections vs 7.7 percent of those who had received placebo (OR 0.49 [CI_{95} .25 to .92]. (Perl TM et al., Intranasal mupirocin to prevent postoperative *Staphylococcus aureus* infections. *N Engl J Med* 2002; 346: 1871-7)**.**

In a 2010 report of a clinical trial in preoperative nasal carriers of *S. aureus* using either nasal mupirocin ointment plus chlorhexidine soap vs placebo, the rate of *S. aureus* infection was 3.4% vs 7.7 %, respectively. The relative risk was 0.42 [CI_{95}. 23 - .75]. **Thus, almost 60% of *S. aureus* SSIs were prevented with current control of the microbiota of the nares and skin.** The effect was more pronounced for deep surgical infections with a risk ratio of 0.21 [CI_{95}. 07 to .62]. (Bode et al., Preventing surgical-site infections in nasal carrier of *Staphylococcus aureus, N Engl J Med* 2010; 362: 9 – 17).

In a cohort of 272 orthopedic patients in which risk factors for SSIs were examined, the only independent predictor of SSI due to *S. aureus* was high – level nasal carriage of *S. aureus* (P=0.002). (Kalmeijer et al., Nasal carriage of staphylococcus aureus is a major risk factor for surgical-site infections in orthopedic surgery, *Infect Control and Hosp Epidemiology* 2000; 21:319-23).

In a double-blind, randomized, placebo – controlled study among orthopedic surgical patients (N=614), eradication of nasal carriage of *Staphylococcus aureus* was 83.5% among those who were treated preoperatively with nasal mupirocin vs 27.8% in placebo recipients. All patients had prosthetic implants for hip, knee or back surgery. <u>The rate of endogenous infections was 5 times lower in the mupirocin group (0.3%) vs the placebo group (1.7%).</u> The total *S. aureus* SSI rate was 1.6% for the mupirocin group vs 2.7% for the placebo group. RR.59 (.20 – 1.79) – 63% reduction but not statistically significant. (Kalmeijer, et al., Surgical Site Infections in Orthopedic Surgery: The Effect of Mupirocin Nasal Ointment in a Double-Blind, Randomized, Placebo-Controlled Study, *Clin Infect Dis* 2002; 35(4): 353-8).

The above data have prompted one team of orthopedic surgeons recently to state that "for patients undergoing surgery requiring a prosthetic implant, nasal colonization with *S. aureus* is the most important independent risk factor for the development of an SSI." Goyal et al., Methicillin – resistant *Staphylococuss aureus* (MRSA), Colonization and pre-operative screening. (*Bone Joint J* 2013; 95-13: 4-9).

In a cross-sectional analysis of *S. aureus* nasal colonization in 284 orthopedic patients preoperatively, Price et al found that 30% carried *S. aureus* of whom 6% were MRSA; by 2005, 4% of such patients were MRSA carriers preoperatively. Of 282 evaluable patients, 9 (3.2%) developed infection. Five of 9 occurred in the arthroplasty group (N=94), four had *S. aureus* – 3 MSSA and 1 MRSA. (C.S. Price et al, Staphylococcus aureus Nasal Colonization in Preoperative Orthopaedic Outpatients, *Clin Orthop Relat* Res 2008; 466:2842-7).

The risk of infection following colonization with MRSA was found to be 4-fold greater than with MSSA colonization – in a review of 10 observational studies of 1170 patients. (Safdar et al, The

Risk of Infection after Nasal Colonization with Staphylococcus Aureus *Am J Med* 2008; 121; 310-15).

The risk of subsequent prosthetic joint seeding after a *S. aureus* bacteremia is also very high: David Murdoch and colleagues prospectively examined 57 patients with prosthetic joints who developed *S. aureus* bloodstream infection: 15/44 or 34% developed a prosthetic joint infection as a result. This contrasted with 1/15 or 7% with other not joint orthopedic devices. (Murdoch et al., Infection of Orthopedic Prostheses after Staphyloccus aureus Bacteremia, *Clin Infect Dis* 2001; 32(4):647-49).

Note: For general surgery and surely for orthopedic implant surgery, it is critical to eliminate *S. aureus* SSI and controlling the microbiome of the nares is key to minimizing *S. aureus* SSIs.

As shown above, in the last 15 years it has been shown that intraoperative warming decreased SSIs by ~ 65 – 75% from the baseline. Because warming is linked to increased subcutaneous tissue oxygenation, the data are consistent with the idea that the microbiome of the skin (numbers or composition or function) is better controlled with perioperative warming.

The data on nasal carriage alone show that control of the microbiota of the nares can incrementally reduce *S. aureus* SSIs by ~60% - 84%. This organism alone comprises 13% - 42% of prosthetic joint infections (Figure 5).

In the Bode et al study in which *S. aureus* SSIs were reduced by 60% with mupirocin and chlorhexidine skin washes, that reduction accounted for an absolute reduction of SSI of 7.5%.

If control of the microbiome of the skin currently has a residual SSI proportion of 20 – 40% (figure 5), addition of nasal mupirocin preoperatively would reduce the residual by almost 10% more. Thus, the updated residual proportion of SSI might be ~ 10% to 30% in 2017 with current control of the microbiome of the skin and nares. **The point is that the vast majority of SSIs are currently recognized by available techniques to be endogenous – from the patients themselves, and studies show that SSIs can increasingly be controlled with better control of patients' microbiome.**

g) Newer Data on the Microbiome

In recent years it has been shown some patients (~20%) carry MRSA in the throat only – not in the nares. Since nasal carriage of *S. aureus* including MRSA is a risk for subsequent SSIs and since no routine perioperative protocol examines for or tries to eliminate throat carriage of *S. aureus* it is reasonable to propose that such carriage could be a risk for SSIs. (See Dalziel, et al., Nasal and Pharyngeal Carriage of Methicillin-resistant Staphylococcus aureus (MRSA) in Undergraduate Nursing Students, www.Asmoline.Education.com/php/ASM 2014; and Mertz et al, Throat Swabs Are Necessary to Reliably Detect Carriers of Staphylococcus aureus, *Clin Infect Dis* 2007 43:475-77; and Mertz, et al, Exclusive Staphylococcus aureus Throat Carriage, *Arch Intern Med* 2009; 169(2): 172-178). Of interest 3-29% of intubated patients develop a transient bacteremia with organisms usually found in the mouth, including *S. aureus.* (See Rijnders et al., Frequency of transient streptococcal bacteremia following urgent orotracheal intubation in critically ill patients, *Intensive Care Med* 2001; 27: 434-37; *Gerber, et al., Risk of*

bacterermia after endotracheal intubation for general anesthesia, Southern Medical Journal, 1980; 73(11): 1478-80)

Valdes, The incidence of bacteraemia associated with tracheal intubation, *Anesth* 2008; 63: 588-92
Konstantinou et al., Difficult intubation provokes bacteremia, *Surg Infect* (Larchmt) 2008; 9 (5): 521-4
In the same concept, A.J. Preston et al showed that 43% of elderly patients admitted to acute care hospitals carry gram negative rods in their oral cavities. No studies have examined the throat as a source for SSIs due to Gram negative bacteria. (See Oral Flora of Elderly Patients following Acute Medical Admission, See Gerontology 1999; 45: 49-52).

A 2015 Danish study showed that there are organisms present in the nasal microbiota below the culture threshold and identified only by finding their genes. Each 10 fold increase in *S. aureus* gene density increased the probability of a positive culture by 30%. So culture of the nares – an insensitive lab test- may underestimate true carriage of *S. aureus.*

Furthermore, in studies of bacterial genes the authors found distinctive prevalent bacteria not known previously to dominate the nasal microbiome including Proteus and Serratia (See Liu et al., *Sci Adv* 2015; e 1 400216). Some information suggesting an expanded role of the nares as a source of SSI, comes from the data of Phillips et al (Phillips, et al., Preventing Surgical Site Infections: A Randomized, Open-Label Trial of Nasal Mupirocin Ointment and Nasal Povidone-Iodine Solution, Infect Control Hosp Epidemiol 2014; 35: 826-32). The authors randomized 1697 patients undergoing arthroplasty or spinal fusion to topical chlorhexidine wipes with either twice daily mupirocin 2% ointment for 5 days prior to surgery or two 30 second applications of nasal povidone iodine 5% within 2 hours of incision. The study was an open label trial. In the intent to treat analysis, deep SSIs developed in 14 of 855 surgeries in the mupirocin group vs 6 of 842 in the povidone iodine group (p=0.10). *S aureus* developed in 5 of the mupirocin treated group vs 1 in the povidone iodine group (p-0.20). In the per protocol analysis, *S. aureus* deep SSI developed in the mupirocin group vs 0 in the povidone iodine group (p=0.03). Thus, if improved nasal decolonization is confirmed in further comparative studies of mupirocin vs alternatives, infection rates will be reduced further.

The new data are consistent with a broader role of the microbiome of the nose and pharynx in SSIs. So far no study has tried to reduce such carriage and examined the rates of subsequent infection.

Summary

The concept herein is that by controlling the microbiome of the skin, SSIs can be significantly reduced, and failure to control the microbiome will lead to SSIs. Note that the Darouiche study and the Tuuli study data indicate 40 – 45% incremental reductions of SSI, above a baseline from the use of standard povidone iodine skin preps and perioperative antibiotic use. http://www.bjjprocs.bone and joint.org.uk/content/go-b/jupp-1/140.4

The data on nasal carriage of *S. aureus* show a distinct link to *S. aureus* SSI and a significant reduction in *S. aureus* SSI if nasal decolonization occurs. Note that several studies have linked underlying diabetes or obesity with higher nasal carriage of *S. aureus* than those without such conditions.

Depending on the assumptions of the effect of povidone-iodine skin prep, a 40% incremental reduction in SSI, with chlorhexidine – alcohol plus ~ 10% (all *S. aureus*) current reduction in SSIs with mupirocin

plus chlorhexidine preoperative skin washes, the residual SSIs are 10% to 30% of the pre-povidone iodine effect. Such estimates suggest that at least 70% to 90% of the source of SSI can already be explained by studies of the patients' microbiome.

The plaintiffs have argued that a substantial proportion of SSIs arise from ambient air in the operating room. Current data suggest that reducing the microbiome counts on the skin with improved skin preps and removing the *S. aureus* burden in the nares accounts for 70%- 90% of the source of SSIs. The skin prep data are consistent with the concept that bacteria of the microbiome are already present in the wound soon after the incision during surgery, and there is no need to postulate an airborne rate. This concept is strengthened by the *P.* acnes data after shoulder surgery and after posterior spine repair surgery. The studies of the source of methicillin – resistant *S. Epidermidis* contamination of the sternal wound with CABG surgery also supports the microbiome of the skin as source of infection at the time of incision. Even with the best control of the microbiome available today, the majority of infections are endogenous.

V. Notes on Laminar flow and Rates of SSI

Laminar flow with reduced numbers of bacteria in the operating room air has been heralded as a strategy to reduce SSIs. This section examines the data.

In the remarkable study by Lidwell et al. who examined the effect of laminar air flow in operating rooms, he and his colleagues randomized 8004 patients undergoing THR or TKR. The risk ratio for infection was 2.6 favoring laminar airflow use (CI_{95} 1.8 – 4.2). However, the authors failed to control for the use of perioperative antibiotics which had an even higher risk ratio of 4.0 favoring use of antibiotics for preventing SSIs. (Lidwell, et al., Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomized study, Br Med J (Clin Res Ed) 1982; 285: 10-14). See more detailed notes later.

Subsequently, three studies showed a worse outcome with the use of laminar air flow, more SSIs with laminar airflow:

1) Brandt's retrospective cohort (N=99,230).
   OR 1.63 for THA (1.06 – 2.52)
   OR 1.76 for TKA (0.80 – 3.85)

(See Brandt, et al., Operating Room Ventilation with Laminar Airflow Shows No Protective Effect on the Surgical Site Infection Rate in Orthopedic and Abdominal Surgery, Ann of Surg 2008: 695-700)

2) Gastmeier's Systematic Review
   (over 75,000 TKA and over 120,000 THA)
   OR 1.36 for TKA (1.06 – 1.74)
   OR 1.71 for THA (1.21 – 2.41)

(See Gastmeier, et al., Influence of laminar airflow on prosthetic joint infections: a systematic review, *J Hosp Inf*. 2012, 81:73-8)

3) Hooper's study of laminar air flow and space suits – 10 years' results of the New Zealand Registry
   (LAF in 36% and space suits in 24%)

(See Hooper, et al., Does the use of laminar flow and space suits reduce early deep infection after total hip and knee replacement, *J Bone Joint Surg. Br 2011; 93:85-90)*

Worse outcomes with LAF or space suits for SSIs

	Inf Rate	P
Space suits	.186%	
No space suits	.064%	<0.0001
LAF	.148%	
No LAF	.061%	<0.003
LAF and space suits	.198%	
No LAF and no Space suits	.053%	<0.001

An update on the New Zealand registry (Tayton E.R. et al., The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty, Bone Joint J 2016; 98-6: 334-40) reinforced the earlier message: Laminar flow systems appear to increase risk in TKA. A total of 64,566 TKAs were followed. The multivariate analysis showed that the OR for infection with the use of LAF was 1.6 (CI_{95} 1.04 – 2.47). They also saw an increase in SSIs at 6 months post operatively with use of surgical helmet systems. The data approached significance on multivariate analysis, with no significant difference at 12 months. The authors conclude that there "appears to be no significant benefit obtained from their use."

Peter Bischoff and colleagues preformed a systematic review and meta-analysis of LAF on SSIs (Bischoff, et al., Effect of laminar airflow ventilation on surgical site infections: a systematic review and meta-analysis, Lancet Infect Dis 2017; 17: 553-61). Eight cohort studies after THA (N=330, 146) showed an OR of 1.29 (CI_{95} .98-1.17 p=0.07 for an increased risk); and six cohort studies for TKA (N= 134,368) showed an OR of 1.08 (CI_{95} 0.77 – 1.52, p=0.65). They concluded that there is "no benefit for LAF vs conventional turbulent air in THA or TKA surgery".

An accompanying editorial concluded that "Until evidence is truly provided, the recommendations should not include LAF technology in operating rooms for prevention of SSIs (Weinstein, et al, Laminar airflow and surgical site infections: the evidence is blowing in the wind, Lancet Infec Dis 2017; 17: 472-3).

Of interest, Rabih Darouiche and colleagues performed a small prospective, clinical trial in which 294 patients undergoing total hip arthroplasty, instrumental spinal procedures or vascular bypass graphs were randomized to an air barrier system or not. The intervention shields open surgical wounds from airborne bacteria. There were significantly lower particulate and CFU densities in the intervention group. Furthermore, CFU density was significantly related to deep implant infections (p=0.021) but not to incisional infections. All four implant infections were in the control group. This study examined a small pocket of air close to the incision. An unanswered question is if the organisms come from the patient's own microbiome or possibly the OR team. Organisms found in the air were not analyzed to compare with those found in the implant infection (MRSA in 1, MSSA in 2, multiple species in 1). As a result, there was a correlation shown between numbers of bacteria in the air and the probability of deep SSIs. The data fail to show cause and effect, however. (Darouiche et al., Association of Airborne Microorganisms in the Operating Room With Implant Infections: A Randomized Controlled Trial, Infect Cont Hosp Epidemiol 2017; 38: 3-10).

If airborne contamination could be linked to implant infections, a critical question is whether a forced air warmer or a comparitor would increase airborne counts.

- Quite recently Oguz and colleagues examined airborne bacterial contamination during minor orthopedic surgery (N=80 patients). They randomized patients to either a forced air warming patients (Bair Hugger) or an electric warming system (Hot Dog). In a multivariate analysis, they showed that absence of laminar airflow and longer duration of surgery increased bacteria in the air significantly. However, the type of warming system had "no significant influence on bacterial counts on any sampling site." (Oguz R. et al. Airborne bacterial contamination during orthopedic surgery: a randomized controlled pilot trial. *J Clin Anesthesia* 2017; 38: 160-64).

The current data strongly support the patient's microbiome as the key source of SSI in clean surgery. There has been debate since the Lidwell study as to the route of infection of the wound. However, a large volume of data suggest that the airborne route is not important. A key factor relative to the Bair Hugger is the prospective study by Oguz and colleagues in clean orthopedic surgery comparing the Bair Hugger to the Hot Dog warmer. Warming with either device had no influence on bacterial counts at any sampling site.

Ayliffe and others have shown that bacterial counts in the operating rooms are directly related to OR activity (Ayliffe, C. A. J. 1991. Role of the environment of the operating suite in surgical wound infection. Rev. of Infec. Dis. 13(Suppl 10):5800-5804). Subsequently the CDC, Joint Commission and AORN have guidelines recommending restricted traffic in ORs, (Mangram, et al, Guideline for Prevention of Surgical Site Infection, 1999, Infect Cont Hosp Epidemiol 1999; 20: 247-80; Spruce, Back to Basics: Preventing Surgical Site Infections, AORN in 2014; 99: 600-611). Until recently many also argued for LAF, since LAF systems reduce bacterial counts. Just as the efficacy and safety of LAF systems have been challenged, so recently has the role of operating room traffic as a significant cause of SSIs have been challenged.

Bohl and colleagues performed a prospective cohort study of 1944 neurosurgical cases and a subsequent randomized single blinded, controlled clinical trial (N=1116) assigning half of the surgeons to regular traffic and half to a low traffic protocol (Bohl et al, The Barrow Randomized Operating Room Traffic (BRITE) Trial: An Observational Study on the Effect of Operating Room Traffic on Infection Rates, Clin Neurosurg 2016; 63; 91-95). In the cohort study, there was no significant difference in total door traffic route between the SSI and non-SSI group; paradoxically, there was a lower infection rate ($p<0.001$) with higher main-door traffic. In the randomized trial, the authors again found a paradoxical trend toward higher SSI risk in the low traffic protocol (3.2% vs high traffic 1.5%, p-0.06). The p value for "take backs" to the OR were respectively 3.1% vs 2.1% p=0.09). The authors concluded that the potential benefits of OR restrictions in reducing SSI rates in, at best trivial and is possibly nonexistent.

So far there are no compelling data linking airborne organisms in the operating room to SSIs. Four cohort studies and a recent meta-analysis show harm - not benefit - with the use of laminar flow systems. OR activity is linked to higher bacterial counts, yet a recent study shows paradoxical benefit with increased main door traffic. Further studies of traffic are needed to confirm the initial findings. A small study (4 deep infections) with a new device to control air near the operative site links bacterial and particulate counts to probability of deep joint replacement infection but no microbiological air and wound cultures were performed. A study of operative room bacteria in the air with Bair Hugger vs HotDog devices in orthopedic surgery shows no contribution to CFUs with either.

Early Studies on Ultraclean Air: Lidwell and Colleagues – 1980s

- Notes on Lidwell OM et al MS, "Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacements: a randomized study." (*Br Med J* 1982; 285: 10-14).

This was an ambitious study of over 8000 patients from 19 hospitals in England (n=11), Scotland (n=4) or Sweden (n=4). The study took 5 years to complete. Those operated in ultraclean OR air had a crude infection rate of 0.6% vs 1.5% in those in turbulent OR air (RR 2.6 and Cl_{95} of 1.6 to 4.2).

The study was flawed, unfortunately, with surgeons' optional use of antibiotics preoperatively, which had an infection RR of 4 (Cl_{95} 2.6-6.2): 0.6% infection rate with antibiotics vs 2.3% without perioperative antibiotics. In the turbulent OR only groups, the risk of infection without antibiotics was 3.4% vs 0.8% with antibiotics for a RR of 4.2.

From table 4- looking only at those patients in ultraclean OR air rooms there were 26 infected among 2120 (1.2%) not given antibiotics vs 20 of 5526 (.36%) among those on antibiotics, a RR of 2.41.

It appears that antibiotics had a greater impact than ultraclean air; yet ultraclean air plus antibiotics had a somewhat lower RR than turbulent air plus antibiotics 3.42 vs 4.2.

Other comments:

Much can change over a 5 year study period including improved technique, and the authors in the introduction note an attack rate for infection "as high as 10%: and with other surgeons very low. "The skill of the surgeons was not accounted for in this study." The timing of reported infections (month and year of study) would have been useful to know to see if skill improved over time. One hospital (in group 1) of the 19 hospitals accounted for one-third of all cases of sepsis, and in the entire study 40% of isolates were *S. aureus*. Thus, a common source outbreak or cluster might have accounted for the findings, which was not investigated.

There was no uniform method of random allocation (page 11).

- Notes on Lidwell O.M. et al MS: "Airborne contamination of wounds in joint replacement operations: The relationship to sepsis rates." *J Hosp Infect* 1983; 4:111-131.

A further analysis of the data from the 1982 publication focused on the correlation of the numbers of airborne bacteria and joint sepsis rates as well as correlations between the numbers of airborne bacteria and numbers of bacteria from wound washouts.

Approximately 20 air samples were taken at each of the 15 hospitals studied for each ventilation-clothing combination (ultraclean vs conventional, and conventional clothing vs body exhaust systems). This was ~ 10% sample of operations and 42 ventilation – clothing combinations. The authors lumped 6 to 9 of the 42 combinations into 6 groups. Thus, some surgeons and hospitals were represented in several of the 6 groups.

In each hospital the number of colony forming units was counted and the mean for each ventilation-clothing combinations noted. Subsequently, a geometric mean of the means was calculated for the 6-9 hospitals in each combination and used for the correlation with infection rates for each of the 6 groupings.

Crude correlations were made, and the authors performed a number of regressions to define the relationships arithmetically between the geometric means of airborne bacteria and the lumped infection rates of the 6 hospital groupings.

It should be noted that the geometric means were crude numbers and there was **no detailed study to show that any specific organism in the air was linked to an organism causing an infection in a specific patient.**

The bigger problem relates to the original flaw – failure to correct for the use of preoperative antibiotics, which could affect both the mean number of bacteria in the wound and in the air. The authors agree (p123), "the colony counts were also less when prophylactic antibiotics had been given," and also **(p126), "similarly, the reduction in the numbers of bacteria in the wash-outs associated with the use of antibiotics is similar to the 4:1 reductions in the incidence of sepsis among patients who received prophylactic antibiotics" (Lidwell et al 1982).**

There is an untested assumption in this paper i.e. that bacteria found in the air later fell into the wound. It seems possible that in operations where there are drills, saws, suctioning, and cautery, the organisms in the wound are splashed into the air. As such the control of the microbiome with perioperative antibiotics would have reduced the numbers of bacteria in the wound and thus subsequently, those in the air.

Other comments:

Though the authors predict that 90% of infections derive from the OR air, this has been easily discredited with current empirical studies. (See Bode et al *NEJM* 2010; 362:9-17 and Darouiche et al *NEJM* 2010; 363: 18-26). In their correlation model the number of organisms in the washout of the wound (W) is the sum of contamination (D) plus non-airborne contamination (K) plus the number found in the air (A). The authors never measured K and in the model assume it is low. Thus, A will be disproportionally high, yielding a falsely high ratio to W. Most importantly, **no infection dose was ever measured and no airborne count linked to specific infections**.

- Notes on Lidwell OM et al MS, "Infections and sepsis after operations for total hip or knee-joint replacement: influence of ultraclean air, prophylactic antibiotics and other factors." *J Hyg Camb* 1984; 93: 505-529.

The authors now focused on wound infection and sepsis not involving the joint, some differences in outcomes for knee vs hip surgeries, and the influence of underlying rheumatoid arthritis. 17% of patients had rheumatoid arthritis, but in 7/19 hospitals the prevalence exceeded 20% (maximum 34%) In the remaining hospitals (12/19) it was under 13% (low of 1%).

The authors state clearly (p.510), "Reasons have been given for believing that the apparent large reduction in the risk of joint sepsis was for the most part genuinely due to effects of antibiotics."

From Table 1:

Antibiotics in control group – 24/2968 became septic; antibiotics in ultra clean group – 9/1279 became septic (p value 0.85 not significant Fisher's exact test). Thus, so long as antibiotics were given, lower rates were seen compared with the no antibiotic group. However, no significant difference in antibiotic group with conventional air vs the antibiotic group with ultra clean air. Thus, no incremental boost was seen with ultraclean air.

Thus, the statement in the summary "the effects of ultraclean air and antibiotics were additive," (p. 505) is not substantiated. The authors also stated (p. 507), "the reduction in bacterial contamination of the wound due to a cleaner atmosphere and the increased resistance to infection from the use of antibiotics appear to combine together independently and multiplicatively."

A key point was made by the authors (p. 518), **"when followed by joint sepsis, the incidence of major sepsis for operations done without antibiotic prophylaxis was 7.9 times that for operations done with such prophylaxis; and the incidence for operations done in conventionally ventilated operating rooms was 2.8 times that for operations done in ultraclean air."**

	Antibiotics	No Antibiotics
Conventional Air	Major 0.6% Minor 3.7% Infection Rate	Major 2.3% Minor 5.1 % Infection Rate
Ultraclean Air		Major 0.7% Minor 5.2% Infection Rate

Thus, the role of major sepsis is the same in ultraclean air with no antibiotics as in conventional air with the use of antibiotics. It appears that ultraclean air had no effect on minor infection in the absence of antibiotics.

85 patients had "suspected joint sepsis" but were not re-operated on. Though the authors' surmise that the majority were in fact infected, clinical experience is that if infected, almost all would need reoperation in order to be cured.

S. aureus isolated in 258 cases

Phage typing in 115 of 258 cases

36/115 : matched the phage type of a person in OR

55/115 : no match with a person in OR

24/115: 18/nontypable with similar characteristics of those of people in OR

9/18 involved one surgeon

6/24 – possible match to a person in OR

A more detailed – examination in from table 8:

Of 115 *S. aureus* isolates:

23 were probably from patient (20%)

2 were probably from surgeon (2%)

11 were probably from assistants (10%) and an additional

6 were possibly from patient (5%)

9 ½ were probably from surgeon (8%)

8 ½ were probably from assistants (7%)

55 – no source found

Probably or possible from patient - 25%
Probably or possible from surgeon - 10%
Possible or probably from assistants - 17%

The authors found the risk of joint sepsis among rheumatoid arthritis patients to be double that for patients without rheumatoid arthritis. This was not corrected for in the primary analysis.

The authors state (p.522) that, "The outcome of the operation improved generally over the period of the study." The magnitude of the effect (p.527) corresponded to an average fall of ~ 50% from the first to third year.

It appears that the data show that ultraclean air influences only severe wound infections whereas prophylactic antibiotics influence both severe and milder infections (p. 525).

Of interest the authors state that the "use of cloxacillin or flucloxicillin alone did not appear to affect the incidence of joint sepsis associated with intestinal – type organism, but that this was reduced or eliminated when wide spectrum antibiotics were given…." In general, intestinal organisms are uncommonly found in the air. If cleaning the air was a critical factor, these intestinal organisms – assumed to fall into the wound from the air - would also be reduced. Instead, the data show that the patients' microbiome was the problem, that failure to control the intestinal organisms was the result of inactive preoperative antibiotics for these (Gram negative rods). On the other hand the antibiotics used would be expected to reduce Gram positive cocci e.g. staphylococcus and streptococcus and substantially reduce infections caused by these. This is exactly what occurred.

If patients develop a SSI after surgery including arthroplasty with organisms that comprise the normal flora of their skin and nares, for some reason their microbiome was not completely controlled. The next question is, can we differentiate the high risk patients for a SSI from those at lower risk. The discussion of risk factors for SSI follows.

VI. Risk Factors

a) **Markers of elevated rates of SSIs. Risk factors are those features of the patients or of the elements of their care that increase or decrease the expected baseline rate of disease.** They help explain the answer to the question, why do some people get an illness such as an infection and others do not. Risk factors are often identified by comparing those with an illness with those who did not acquire the illness in what are referred to as case - control studies. In such studies the cases and controls are examined for the potential risk factors in a defined number of days prior to infection in the case. In retrospective studies, they are quantified by *odds ratio* – a comparison of the odds of infection for example – among those exposed to "X" to the odds of infection among those not exposed to "X".

In the U.S., approximately 1 million patients undergo prosthetic joint implants each year and ~ 1% develop a prosthetic joint infection. Risk factors identify those at higher risk for a SSI. Once it is established that a risk factor for infection exists, efforts to reduce the exposure are made in attempts to minimize or eliminate the infection.

For decades, anesthesiologists have gauged a surgical patient's fitness for surgery using the ASA (American Society of Anesthesiologists) score preoperatively:

ASA Score

1. Healthy

2. Mild systemic disease (well controlled disease of one body system)

3. Severe systemic disease (controlled disease of more than one body system)

4. Severe systemic disease that is a constant threat to life

(See http://my.clevelandclinic.org/health/treatments - and procedures/regarding ASA score).

The Centers for Disease Control and Prevention (CDC) subsequently utilized the ASA as an element in their risk assessment for SSIs:

CDC NNIS Risk Index Score No. Points	SSI Risk	Criteria for CDC NNIS Points:
0	1.5%	1 – if contaminated or dirty surgery
1	2.9%	1 – if ASA ≥ 3
2	6.8%	1 – if op time exceeds the 75th percentile for that procedure (>3 hour for joint replacement)
3	13%	

See Pear SM. Patient risk factors and best practices for surgical site prevention managing. *Infect Control* 2007 (March):55-64

An ASA score >2 was also shown to be an independent risk factor for periprosthetic joint infection in a study of 9245 patients undergoing primary hip or knee arthroplasty – odds ratio 1.95 (CI_{95} 1-3.7) (L Pulido et al *Clin Ortho Relat Res* 2008; 466: 1710 - 15).

A Duke University case – control study of elderly surgical patients (age 65 or older) showed the following to be significant independent risk factors for a surgical site infection:

Variable	Odds Ratio (CI_{95})
Obesity	1.77 (1.34 – 2.32)
COPD	1.66 (1.17 – 2.34)
Contaminated or Dirty Surgery	1.65 (1.0 – 2.72)
Private Insurance	0.29 (0.12 – 0.68)

The study included 569 SSI cases and 580 controls; 18% had orthopedic infections. (Kay K. et al J Am Geriatr Soc 2006; 54: 391-396).

As an example of how to interpret the data is that the presence of obesity increased the risk for a SSI by 77% above the baseline. The statement that these are independent risk factors means that the estimates are already controlled for the presence of other potential risk factors, including COPD.

Infection of the Surgical Site after Arthroplasty of the Hip: Independent Risk Factors

Number of THA = 16,291
Rate of SSI = 2.23%
Ridgeway S et al J Bone Joint Surg (Br) 2005; 87: 844-50

Multivariate Analysis of Risk Factors for SSI

	Variable	OR	CI_{95}	P
Trauma	No	1		
	Yes	1.87	1.5 – 2.34	<0.001
Age	<65	1		
	65-74	1.13	.85-1.5	
	74-79	1.56	1.16 – 2.10	
	≥80	1.66	1.24 – 2.21	0.001
ASA	<3	1		
	≥3	1.55	1.29-1.88	<0.001
Duration of Surgery (Min)				
<60		1.04	.82 – 1.34	
60-90		1	Baseline	
90-120		1.23	.96-1.57	
> 120		1.58	1.23 – 2.03	0.004

Trauma, older age, higher ASA, and longer surgery time each predicted an above average risk for SSI.

Risk Factors for SSI

MA Olsen et al. Risk factors for surgical site infections following orthopedic spinal operations *J Bone Joint Sgy* 2008; 90: 62-9

Case Control Study
46 Infected and 227 uninfected controls: rate SSI – 2%

Independent risk factors

Risk Factor	OR	CI_{95}
DM	3.5	1.2 - 10
Preop Glucose > 125 mg/dl % or postop 200 mg/dl	3.3	1.4 – 7.5
Obesity	2.2	1.1 – 4.7
≥ 2 surgical Residents participating	2.2	1 – 4.7
Suboptimal timing of antibiotics	3.4	1.5 – 7.9

Key: DM= Diabetes mellitus
OR= Odds ratio
CI_{95}= 95 percent confidence interval

- This study is relevant to orthopedic surgery. With the presence of diabetes mellitus, a preoperative glucose over 125 mg/dL and obesity, a patient would have a higher than average risk of acquiring a SSI. Independent risk factors such as those found in a logistic model that are present in the same patient are additive. In this model such a patient would have a very much increased surgical site infection risk compared to patients without such risk factors by virtue of his diabetes mellitus, a preop glucose over 125 mg/dl and obesity. His risk would be 3.5 + 3.3 + 2.2 or 9 times greater than patients without any of these three risk factors.
- If the baseline rate of infection is 1% or 1.5% or 2%, that patient's predicted infection risk would be 9%, 13.5% or 18%, respectively – without considering other risk factors for infection.

Another case control study confirmed the importance of diabetes as a risk factor with an OR of 3.91 (P=0.04) Lai et al J arthroplasty 2007; 22:651-6

Importantly, Dowsey MM et al showed the outcome among patients who were both diabetic and obese in a study of 1214 consecutive primary total hip arthroplasties
Clin Orthrop Rel Res 2009; 467: 1577-81
Total infection Rate 1.5% (N=18)

Variable	OR	CI_{95}
Morbid Obesity	8.96	1.59 – 50.63
Diabetes	6.87	2.42 – 19.56
Men	5.93	1.95 – 18.04
Surgical Drainage	0.24	0.06-0.95

Of interest, there were no prosthetic joint infections (PJI) among diabetics who were not obese; 11 PJI if both diabetes and obese; 4 PJI if obese but not diabetic.

Smoking as a Risk Factor for Surgical Site Infections after Orthopedic Implant Procedures

Title: Smoking is a risk factor for organ/space surgical site infections in surgery with implant materials
Authors: F. Duran et al
Journal: int Orthop 2013; 37: 723-7

Largest orthopedic cohort studied: 17 French hospitals and 3908 patients; smokers comprised 16.4% and non-smokers 83.6%
59% THA and 30% TKA with 11% others

- Multivariate analysis of predictors for SSI in the 12 month follow-up: smoking had an odds ratio of 2.2 with CI_{95} of 1.4 – 3.7.

Comment: The model suggests that smoking, independent of other risk factors, doubled the baseline risk a surgical site infection after a joint replacement.

Alcohol Consumption and the Risk of Nosocomial Infections in General Surgery

Prospective study of 1505 patients Delgade-Rodriguez M. et al
BR J Surg 2003; 90: 1287-93

Men and heavy alcohol consumption
(Defined as over 108 Grams/d) increased the rate of all site nosocomial infections: Odds ratio 2.51 (CI_{95} 1.06 – 5.96), and in hospital Surgical Site Infections: odds ratio 2.16 (CI_{95} . 84-5.59 – NS)

Health Care Associated Infections in Surgical Patients Undergoing elective surgery: Are Alcohol Use Disorders a Risk Factor?

(de Wit, et al, Health Care-Associated Infection, J Am Coll Surg 2012; 215:229-36).

Over 1 million patients evaluated: Hospital acquired infections in 38,335 (3%); Surgical site infections in 0.5%
Alcohol abuse in 0.9% (11,640 patients)

Hospital acquired infections and Surgical Site Infections were strongly associated with heavy use, respectively:
Odds ratios, respectively of 1.7 and 2.73 ($P < 10^{-6}$)
Heavy drinking defined > 4 drinks/day or over 14/week for males

Comment: The data suggest a doubling of infection risk with heavy alcohol consumption alone.

In a study of comorbidities in patients with infected hip or knee arthroplasties, Lai and colleagues should that each of numerous medical comorbidities increased the risk of infection by 35% (OR 1.35 in univariate analysis); because this variable was linked to all other medical conditions, it was not entered into the adjusted analysis. In the latter the odds ratio for diabetes, an independent predictor, was 3.91 (1.06 – 14.44), p 0.041. (J Arthroplasty 2007; 22: 651-6).

CC Sheth and colleagues showed that alcohol and tobacco consumption affect the oral microbiome, specifically the carriage of *Candida Albicans* and *Streptococcus mutans*. (See Sheth, et al., Alcohol and tobacco consumption affect the orial carriage of Candida albicans and mutans streptococci, *Lett Appl Microbiol* 2016; 63: 254-9). Saliva samples of 105 patients were studies and patients stratified by duration and quantity of alcohol and tobacco consumption. Tobacco users harbored elevated levels of *C. Albicans* and alcohol consumption statistically significantly decreased the oral carriage of *S. mutans*. Such studies suggest that the microbiome is altered with some recognized risk factors for SSIs. More studies are needed on surgical patients, however.

In a cross sectional study of 20 women smokers and 20 women nonsmokers, RM Brotman and colleagues showed that smoking was linked to a lower proportion of vaginal lactobacillus species vs nonsmokers. That species has been thought to be part of a protective microbiome, and decline of lactobacillus carriage is linked to bacterial vaginosis. No surgical patients have been studied. (See Brotman, et al., Association between cigarette smoking and the vaginal microbiota: a pilot study, *BMC Infect Dis* 2014; Aug 28; 14: 471).

Risk Factors Identified Independent of the Bair Hugger Use

In the clinical trial using the Bair Hugger vs no Bair Hugger independent risk factors from multivariate analysis showed the following risk factors – after controlling for the use of the Bair Hugger (See Kurz, et al, Perioperative Normothermia to Reduce the Incidence of Surgical-Wound Infection and Shorten Hispitalization, *N Engl J Med* 1996; 334:1209-15).

Risk Factors	OR	CI_{95}
Tobacco Use (yes vs no)	10.5	3.2 – 34.1
NNIS Score (per unit increase)	2.5	1.2 – 5.3
Age (per decade)	1.6	1.0 – 2.4

In this study smoking, higher NNIS score and age were risk factors for infection independent of the use of the Bair Hugger. If a patient was a smoker, whether or not she used the Bair Hugger, she would have an odds ratio of 10.5 for infection. If the baseline rate was 1% or 1.5% or 2.0%, that person's risk for a SSI would be predicted to be 10.5%, ~16% or 21%, respectively, independent of NNIS score or age.

Infections with Prostheses in Bones and Joints - Review

Hematoma as an independent risk factor for prosthetic joint infection. A case control study Saleh K et al. J Orthoped Res 2002; 20: 506 – 15.
Study of THA (N=1181) and TKA (N=1124): 33 Infected Cases and 64 Controls.
Multivariate Logistic Regression.

Variable	OR	CI_{95}
Hematoma	11.78	3.02 – 46.03
Days of Drainage	1.32	1.08 – 1.62

Definition of hematoma: subcutaneous palpable collection of fluid or mass

- These data alone suggest that a patient with a hematoma increased his or her risk of infection ~12 – fold greater than patients without a hematoma.
- In this model the presence of a hematoma would predict a risk of infection of ~ 12%, 18% and 24%, respectively, if the baseline rate of infection is 1% or 1.5% or 2%, respectively. If one Thrombopophylaxis agent was more likely after THA or TKA to cause bleeding into a wound (hematoma), one would not be surprised to see an accompanying elevated SSI risk.

Surgical volume at an institution has been linked to risk of SSIs. Specifically, low volume hospitals have higher rates of SSIs, than high volume hospitals. In a recent report of Medicare patients undergoing THR from 2005-2011 with an annual number of replacements of 21,000/year, the relationship held:

THR Procedures/yr.	AOR (CI_{95})
1 – 24	1.58 (1.47 – 1.09)
25 – 49	1.34 (1.26 – 1.44)
50 – 99	1.22 – (1.15 – 1.30)
100 – 199	1.14 (1.07 – 1.21)
200 +	Ref

M. Calderwood et al Med Care 2017; 55: 179-85. These data suggest that patients' risk of a PJI increase as the number performed at a hospital declines. Best results were in institutions that did at least 200 per year.

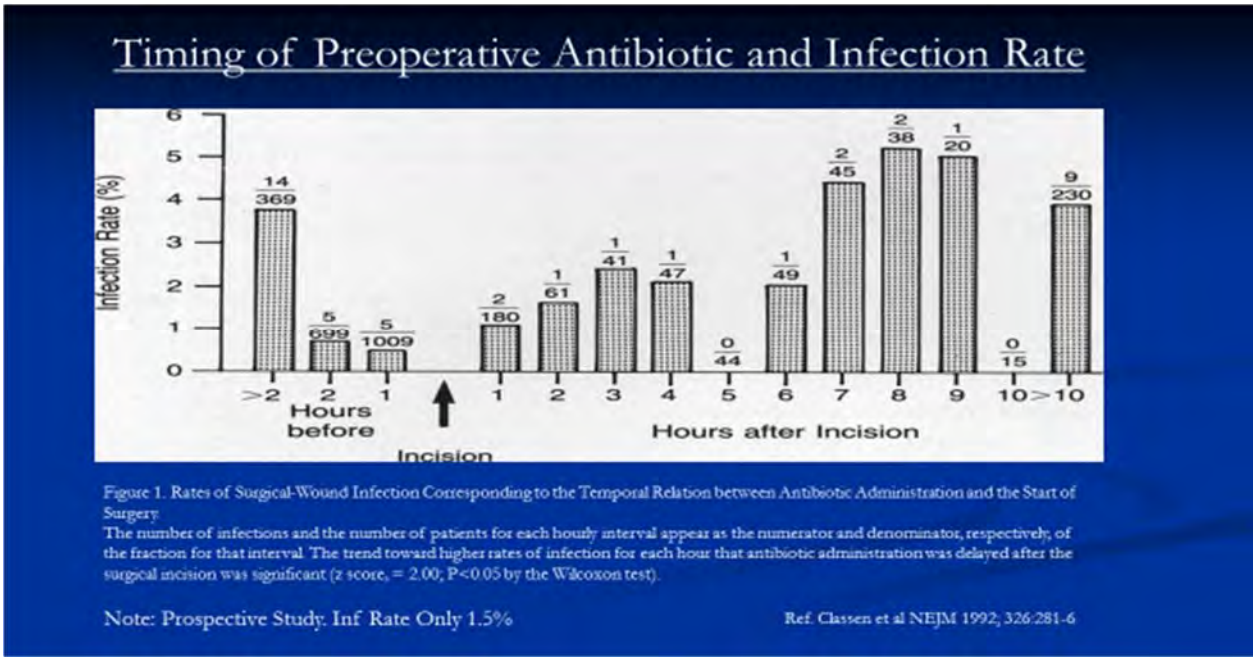


Figure 8

The timing of perioperative antibiotics has been shown to be important in preventing SSIs in general, with best results if given within 2 hours of the incision. (Figure 8)
(Classen, et al., The Timing of Prophylactic Administration of Antibiotics and the Risk of Surgical-Wound Infection, N Engl J Med 1992;326:281-6)

The key point is that getting the perioperative antibiotic timing right will reduce SSIs.

More recently most hospitals have targeted the 60 minutes before incision for receipt of perioperative antibiotics, and many in Europe target 30 minutes prior to incision

The data from Van Kastern et al suggest best results (lowest SSI) after THA might be 30 minutes prior to incision. (Clin Infect Dis 2007; 44: 921-7). (Figure 9)

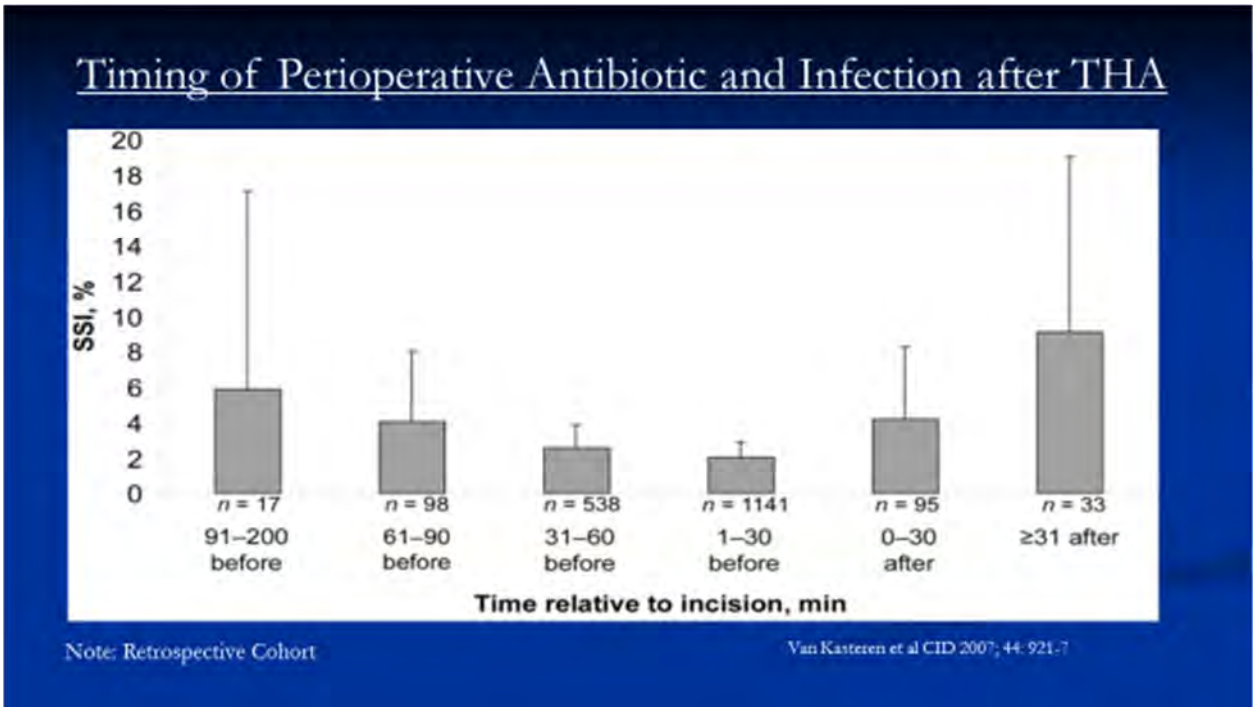

Timing of Perioperative Antibiotic and Infection after THA
SSI, %
20
18
16
14
12
10
8
6
4
2
0
n = 17
91–200 before
n = 98
61–90 before
n = 538
31–60 before
n = 1141
1–30 before
n = 95
0–30 after
n = 33
≥31 after
Time relative to incision, min
Note: Retrospective Cohort
Van Kasteren et al CID 2007; 44: 921-7

Figure 9

Risk factors for Prosthetic Joint Infections: Case-Control Study

Berbari, et al, *Clin Inf Dis* 1998; 27: 1247-54

Mayo Clinic Study by E Berbari: 462 cases matched to 462 controls

Risk Factor	Independent OR	CI_{95}
NNIS Score 1	1.7	1.2 – 2.3
2	3.9	2-7.5
History of same Joint Anthoplasty previously	2	1 – 4.3
Malignancy- not involving the index joint	3.1	1.3 – 7.2
SSI not involving Prosthesis	35.9	8.3 – 154.6

- With a patient's history of a prior hip joint replacement at the same site, this model suggests a doubling of the risk for infection – without considering other known risk factors such as obesity or diabetes.

  Controls were matched for age, sex, prosthesis location, and date of implantation. In addition, the length of follow-up for each control had to be greater than or equal to the interval from implantation to infection in the case.

  The odds ratios were derived from a conditional logistic regression model. Thus, the odds ratios are after a multivariate analysis.

  A recent study by Bedair and colleagues examined the question, if a history of treated prosthetic joint infection increases the risk of subsequent PJI at a different joint. A retrospective matched cohort study included 90 cases successfully treated for a second primary THA or TKA. Controls were matched for age, sex, diabetic status, BMI, ASA score institution, joint of interest and years of surgery (± 2). 10 of 90 controls vs 0 of 90 cases developed a PJI. The RR was 21 and CI^{95} 1.25 – 353.08, p=0.035.
  H. Bedair et al., A history of treated Periprosthetic Joint Infection Increases the Risk of Subsequent Different Site Infection. (*Clin Orthop Res* 2015; 473:2300-4).

Summary

A number of risk factors have been identified that address the question of why some patients get a SSI after the operation and others do not. Among those are preoperative diagnoses such as obesity, diabetes, nasal carriage of *S. aureus*, COPD, elevated preoperative or postoperative blood sugar level, smoking, and excess alcohol intake; and a post-operative hematoma. Process – related risk factors relate to surgeon and institution volume (number of THA and TKA performed per year), timing of perioperative antibiotics and preoperative skin preps. Some models include the presence of several risk factors, and the odds ratio of each patient can be added to get a summary odds ratio and multiply that number by the expected base line infection rate.

Note – Independent risk factors identify those patients having surgery who are at higher risk for a SSI than patients without such risk factors. It is likely that they alter the microbiome. Many surgeons try to control these by asking obese patients to lose weight before surgery, by asking diabetics to control their blood sugar before surgery, and ask smokers to stop smoking before surgery.

Though the science of the microbiome is young, a number of studies have shown changes in microbiome density and composition with the comorbidities listed above as risk factors. It should be emphasized that the presence of nasal carriage of *S. aureus* predicts a 2-3 fold increase in SSIs due to that organism. We know that obesity and diabetes mellitus both influence the microbiome by increasing the patients' prevalence of *S. aureus* carriage. Older patients have a higher carriage of Gram negative rods in their oral cavity, a possible source for SSIs. Some patients carry MRSA in the throat only, a possible source for SSIs and /or a marker of its presence on other parts of the body.

So far, the current data show remarkable safety of FAW including the Bair Hugger and no harm to patients. Current data make a compelling argument for the safety of the Bair Hugger. It is not a risk factor for infection. An unfortunate risk for patients undergoing arthroplasties is a prosthetic joint infection with an organism recognized to be a component of the normal microbiome. Progressive control of the microbiome has had a large impact on reducing SSIs. The currently uncontrolled residual risk of infection can usually be explained by risk factors listed above.

It is important to point out the multifactorial components of infection. Bacteria are a necessary but not sufficient cause. Risk factors address the components that increase risk for some patients. So if no bacterium and no risk factor is sufficient to cause an infection, all are in part risk factors that combine to cause an infection in some patients. If the question is what caused the infection in Mr. Jones, one could point to his organism recovered, his diabetes and obesity and say that all contributed, all caused the infection.

Risk factors thus play a role in SSIs by altering or increasing the bacterial burden in the microbiome and/or possibly by reducing the host's ability to resist her own microbiome or the bacteria from exogenous sources.

VII. Plaintiff's Critique of the Bair Hugger

a. Background – Routes of bacterial transmission from reservoir to operative site

The arguments have been made above for the key reservoir of bacteria implicated in clean surgery SSIs being the patients' microbiome – her own skin and mucous membrane flora.

The next question is how the organisms of the microbiome reach the operative site in most cases. Some possibilities include transient bloodstream infections of oral flora (including *S. aureus*) after intubation. A second possibility is the transmission of elements of the microbiome to the air in the operating room. A third possibility is that in most cases the offending organism is there at the operative site at the time of incision and causes infection directly.

In terms of nasal colonization with *S. aureus,* its presence may imply colonization elsewhere on the body, not just in the nares.

A clinical trial of the efficacy of mupirocin for clearing nasal carriage of *S. aureus* also examined hand carriage in the same people. Stable carriers of *S. aureus* were randomized for 5 days of intranasal mupirocin twice daily or placebo. At 3 months, 71% of subjects receiving mupirocin group remained free of nasal *S. aureus* vs 18% of controls. 30% of the mupirocin group and 50% of controls had *S. aureus* on their hands before initiating therapy. On day 3 of therapy, elimination of carriage was seen in 8 of 10 carriers on the hands of those receiving mupirocin, but only 3 of 16 were eliminated among those receiving placebo. The same fingerprint was noted in the nose and hands was noted in 97% of tests. Thus, a large proportion of nasal carriers have the same organism on the hands and elimination of nasal carriage was associated with elimination on the hands.

In terms of the transient bloodstream pathway, 3 – 29% of patients after intubation develop a bloodstream infection, and organisms could attach to the operative site at that time. Current data suggest the possibility but only a minority of infections seems likely in the face of current data.

In terms of the airborne route of transmissions, the arguments against this would be the finding of worse outcomes after the use of laminar airflow systems are in place – four large retrospective cohorts noted above and a recent critical review and meta-analysis. The studies in neurosurgery patients showing a decrease in SSIs with more main door traffic adds to the growing body of evidence against airborne transmission of the

microbiome. A recent contradictory study using an air shield over the operative site by Darouiche and colleagues – suggested this pathway, although no bacterial cultures of air and wounds were studied to show a true casual pathway. Importantly, a linked question is – if the airborne route of transmission occurs in a minority of cases, does the Bair Hugger increase the risk? In recent clinical trial in which the Hot Dog vs the Bair Hugger were evaluated, warming by either machine did not increase particle bacterial counts in the air in the operating room, suggesting no contribution by the Bair Hugger to risk.

A third possibility is that the organisms of the skin are currently not controlled maximally by skin preps or perioperative antibiotics, and the microbiome is already present at the operative site, causing infections in high risk patients. The data on the high risk of *P. acnes* after shoulder surgery and supportive data on posterior spinal repair surgery would strongly support this idea. The sternal wound contamination studies showing the skin over the sternum as the source of MRSE in CABG surgery further corroborates this concept. The point is that the organism causing contamination and infection of the wound are present at the time of the incision.

The 1963 study by Burke et al – well prior to the use of the Bair Hugger showed strains of *S. aureus* in the wound that matched those in the patients' skin, nose or throat, just prior to closing. These data also are consistent with the concept that the organisms causing infection after surgery are already present in the wound site and unrelated to the use of forced air warmers. These data are consistent with more recent data examining a marker organism, *P. Acnes*, in shoulder surgery (Joint replacement and rotator cuff repair) and posterior spine surgery. This species is commonly implicated in SSIs after the above procedures. Finding them before and immediately after skin preps and after incision and at the end of surgery is compatible with the idea that they are already in the wound at the time of the incision.

b. Particles, air bubbles, filter efficiency and cultures of the Bair Hugger apparatus.

Eight studies have been cited by the plaintiffs relating to the examination of air particles, air bubbles, filter efficiency of the Bair Hugger and cultures of the Bair Hugger. In these experimental studies **which were hypothesis – generation studies, no infection rates were measured, and no link of infection to the Bair Hugger was shown.**

Some studies showed increased numbers of bubbles and particles with the use of the Bair Hugger vs Hot Dog; some showed reduced filter efficiency, and some showed that the inside of the Bair Hugger apparatus had bacterial contamination. No study has shown bacterial contamination in the air from the blanket when the apparatus is in place as it is properly used for surgery. A brief summary of the studies follows:

Particles air bubbles, filter efficiency, cultures of Bair Hugger Apparatus

- Albrecht 2009 -25 FAW – using laser particle counts: 24% found to emit airborne particles. Microorganisms in 94% of internal surfaces; 34% filters had "abnormal" filtration

- Albrecht 2011 – 5 new and 5 used intake filters of Bair Hugger
  Filter efficiency 61% - 94% using sodium chloride aerosol
  92% microbes in air path
  58% generating airborne particles

- Reed 2013 – Intake filter was 64% efficient; swabs-100% FAW had bacteria. Hose end showed particles in 96%

- Legg 2012 – FAW caused increased temperature 1.1° C vs 0.4°C for the Hot Dog; and particles (1038 vs 273) over surgical site
  Volunteer patient in simulated OR with no OR "nurses"

- Legg 2013 – Simulated TKA in theatre. Buoyant helium bubbles counted: Increased particle counts and increased convection currents noted

- Dasari 2012 - Draped manikin in LAF room. FAW increased temp vs Hot Dog by 2.7° C and 3.6° vs resistive blanket

- Belani 2013 - FAW vs Hot Dog – with manikin in ortho OR. Increased neutrally buoyant bubbles with FAW

- McGovern 2011 – Increased bubble counts over surgical site greater with FAW than with Hot Dog and air from floor mobilized

In Mr. Albrecht's deposition , he clarifies his many studies, stating that the airborne particles counted do not reflect bacterial counts (p.65-66); that particles counted out of the Bair Hugger were noted, but not much in the way of bacteria was noted (p 73); that filtration efficiency was based on particle counts coming and leaving but not bacterial counts (p. 103); that in the 3 Minnesota hospitals he and his colleagues found particle emissions with varying efficiency of the Bair Hugger filter and internal surface contamination, but "none looked at the actual bacteria in the airstream." (p.103-104). The table below summarizes the emissions from the unpublished Bair Hugger studies in Minnesota (p. 110):

Institution	Tested No. Units	No. CFU Cultured
St. Cloud	3	0/3
Alexandria	3	6 measurements: 2 had 1 CFU 4 had 0 CFU
Regina	3	9 Measurements: One unit had all zeros Another unit had 1 cfu and 0s in the others Another unit - had 1 cfu on one and two zeros

Mr. Albrecht – in response to why these data were not included in the published studies - says that since the ORs studied were at rest, he and his colleagues were unsure how to interpret the results (p. 113). Two additional studies were also conducted by Mr. Albrecht that were not published. They also showed that no bacteria were noted when the Bair Hugger was in use. Thus, five negative studies were not published (Augustine deposition, pp 53-75 re: Exhibit 8). The question was: "so does this comport with your recollection back in 2007, 2008 time frame, internally Augustine Biomedical + Design tried five different times to capture viable bacteria coming out of the airstream from the Bair Hugger hose, but – and using three different capture techniques, but never captured any meaningful numbers of bacteria?"

Answer: "That's what these reports say" (p. 68).

In Mr. Legg's deposition he added new information related to his particle studies. He and his colleagues attempted to measure bacteria using agar plates in the simulated operating room experiment (p. 53). Specifically, they used agar plates "placed where we were concerned, which was on the surgical site" (p. 54). When asked how many bacteria grew, he responded "less than one" colony forming unit (p. 55), during the time when the Bair Hugger was used. When asked why this information was not reported with the report about the particles, he said that "it didn't really add anything" (p. 5). He later clarified that the standard – set for the orthopedic theatre – is also less than one colony forming unit. When asked to respond to the finding that despite increased particles being mobilized at the operative site, the particles were not adding to the bacterial load, Mr. Legg agreed (p. 58).

In his deposition, Dr. Paul McGovern provided raw data on a number of studies in which attempted to count bacteria or particles in the air of an operating room (volume 8 pp 3539 – 3717) at Wansbeck General Hospital. In 4 experiments the introduction of a surgeon raised the particle count in the zone of the operative field, most marked when the surgeon touched the disinfected skin within the field. "However, there is no suggestion from these results that turning on the Bair Hugger makes any difference to the operative field particle counts" (p. 3547).

Minimal numbers of bacteria were isolated from settle plates opened for 4 hours. Counts of microorganism from settle plates showed mostly zeros (p. 3548). Air samples during the operating procedures also showed zero cfu when the Bair Hugger was turned on (p. 3550). Wound swabbing and sampling Bair Hugger showed "only very low numbers of skin bacteria" (p. 3552). He concluded (p. 3574) that "Use of forced air warming devices does not increase the bacterial count in the vicinity of the operative field."

These data on bacterial counts were never published, and Dr. McGovern and his colleagues chose to pursue studies of particles and had the selective data from the latter experiments published. Asked why the different approaches, Dr. McGovern said that an abstract had been rejected (deposition p. 67), that negative findings are difficult to get published (deposition p.68), and that no statistical significance of the data was taken into account (deposition p. 71).

One is forced to conclude that a large volume of data had shown that the use of the Bair Hugger has no influence on bacterial counts in the operating room. The authors of these studies failed to publish the data and instead appeared to focus on air currents and particles as implied surrogate markers of bacteria counts.

c. The McGovern Study – The Clinical Arm

The McGovern study (*J Bone Joint Surgery* (BR) 2011; 93: 1537-44) is cited by the plaintiffs as a clinical evaluation of the comparison of the Bair Hugger vs the Hot Dog Warming devices with the end point of the rate of prosthetic joint infections. The abstract states that there was an "elevated infection odds ratio of 3.8 (p=0.024)" favoring the use of the Hot Dog.

These were a number of fatal flows in study design and analysis, and **the authors themselves correctly state that "this study does not establish a casual basis for this association."**

The study was a "before and after" observation comparing surgical site infection rates between the Bair Hugger and Hot Dog systems. The method section offers no hypothesis, no study design details to offer a rationale for the study periods for the two warming systems. The authors acknowledge the failure to control for independent risk factors: blood transfusion,

obesity, incontinence and fitness for surgery. They also ignored multiple other factors known to affect infection risk.

Other shortcomings include the following.

- Intraoperative temperatures were not measured, thus a key risk factor was not examined.
- The surveillance systems – case finding methods – were not mentioned, and there are no data on validity of surveillance or in completeness of case finding after patients were discharged. This is especially important in non-contemporaneous comparisons, where observation bias can be introduced.
- There were no data to show that perioperative antibiotics were appropriately timed relative to the incision in the two time periods.
- With the large number of *S aureus* isolates recovered during the forced air period (N=11) vs none (N=0) for the conductive fabric warming, one needs to know what workup was done to rule out an epidemic caused by a single clone. No fingerprinting of isolates was noted.
- One of the coauthors, Mr. Albrecht, worked for the company competing with the Bair Hugger and has a substantial conflict of interest.

An important point with respect to controlling for such confounding factors is that the odds ratio reported is a univariate funding, not corrected for the known confounders of infection. It was not a multivariate analysis but instead a crude examination of incomplete data.

Even more serious flaws involve bias (systematic errors) in the study, which – unlike confounders – cannot be corrected. Bias in a study is a fatal flaw. There were multiple biases in the study, each one of which favored the Hot Dog:

1) Rivaroxaban (Xarelto) anticlotting drug – linked to wound hematomas – was used for part of the Bair Hugger period but <u>never during the Hot Dog use period</u>; (See Professor Holford's analysis).

2) Gentamicin perioperative prophylaxis alone was used for much of the Bair Hugger period yet <u>two antibiotics – gentamicin plus Teicoplanin</u> – <u>were used always during the Hot Dog period</u>. Gentamicin would be expected to have no or little activity for MRSA and for coagulase negative staphylococci. Dr. Reed and co-authors from the Northumbria Healthcare NHS Foundation Trust wrote that "gentamicin 4.5 mg/kg alone should not be used as prophylaxis for primary joint arthroplasty as it…increases the risk of other postoperative complications" increase in pneumonia..acute renal failure requiring HDU admission..and rate of return to theatre." The authors noted trends of increasing resistance to gentamicin among the coagulase negative s*taphylococc*i. In conclusion, they say "we have changed our prophylaxis to low dose gentamicin (3mg/kg) combined with Teicoplanin 400 mg given once."

Sprowson A et al. Changing antibiotic prophylaxis for primary joint arthroplasty affects postoperative complication rates and bacterial spectrum. *The Surgeon* 2013; II: 20 – 24.

It should be noted that the study extended over a 2-1/2 years period during which time 20 months were exclusively for the Bair Hugger followed by an optional warmer for 3 months of transition, then followed by a 7 months exclusive period of use of the Hot Dog. This is a very strange study design, suggesting a late decision to examine data retrospectively.

3) In the Bair Hugger period there was no MSSA screening from 7/01/08 through 12/31/10 (Dr. Reed's deposition page 110), during which time there were 9 pure plus 1 mixed *S. aureus* infections. There were no MSSA in the Hot Dog study period.

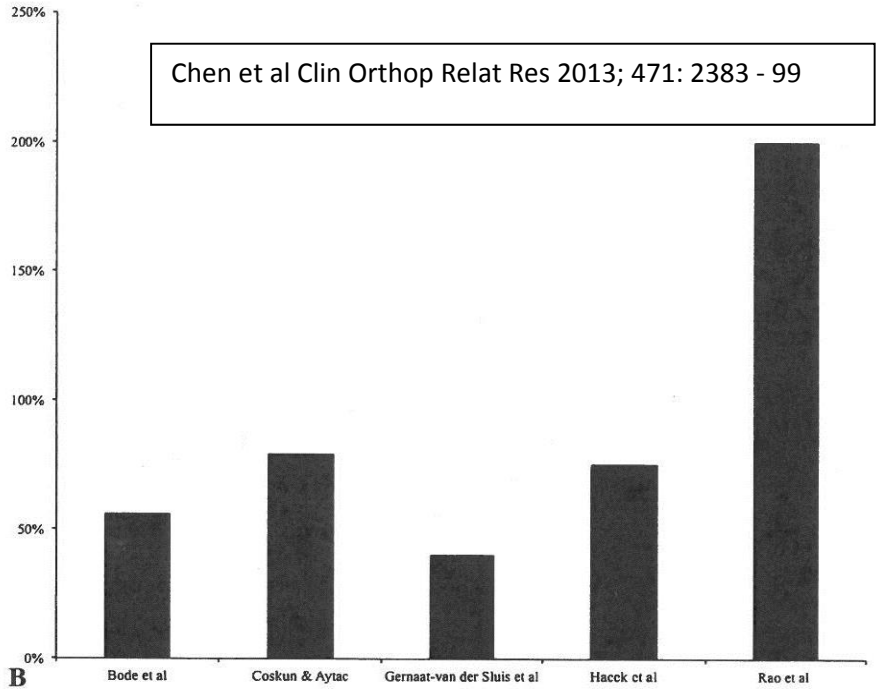
MSSA screening began in January 2010 and was continued thereafter, including the entire Hot Dog period.
A systematic review of *S. aureus* screening and decolonization in orthopedic surgery involving 19 studies showed a reduction of SSIs or wound complications in all 19 (Chen et al Clin Orthop Rel Res 2013; 471: 2583 – 99). Nine of the studies were prospective and 10 were retrospective. Most studies evaluated patients undergoing elective joint replacements.

The reduction of overall SSIs ranged from 13% to 200%; the reductions of MRSA SSIs ranged from 29% to 149%; and the reduction of *S. aureus (MSSA)* SSIs ranged from 40% to 200%. Four of the five studies evaluating *MSSA SSIs showed* ≥ 50% reduction of *S. aureus* SSIs.

Based on the studies above, it is reasonable to suggest that in Bair Hugger period there could have been on the order of a 50% reduction of MSSA SSI, from 10 to 5, had MSSA screening been instituted from 7/01/08.

Figure 10

Chen et al Clin Orthop Relat Res 2013; 471: 2383 - 99



During the Bair Hugger period, there was a THA infection related to *Pasteurella Multocida.* The procedure date was 12/09/08. This was surely community acquired and had nothing to do with what occurred in the operating room. A review of the literature would support dropping this case from the Bair Hugger health care associated infections. Sixteen cases of TKA and two THA sepsis have been reported in the literature almost always caused by a dog or cat bite, scratch or tick. These are most commonly linked to a bacteremia.

Hydeman J et al
Internat J Infect Dis
Acute infection of a total knee arthroplasty caused by Pasteurella Multocida, a case report and a comprehensive review of the literature in the last 10 years.
Before examining methodological study issues, one should drop the case of Pasteurella and correct the misclassification (once fewer in the Bair Hugger period and one more in the Hot Dog period) as noted in discovery.

4) A switch to chlorhexidine – alcohol skin prep was made on October 1, 2010, so only during the Hot Dog period. Since it has been clearly shown that this prep leads to a 40% reduction in all SSIs, a serious bias is present. A 40% incremental reduction in SSIs during the Bair Hugger period would have had an enormous decrease in the infection rate.

In the manuscript that was published, the authors had an illustration of infection rates. The impression was a flat rate over the first 20 months (Figure 11).

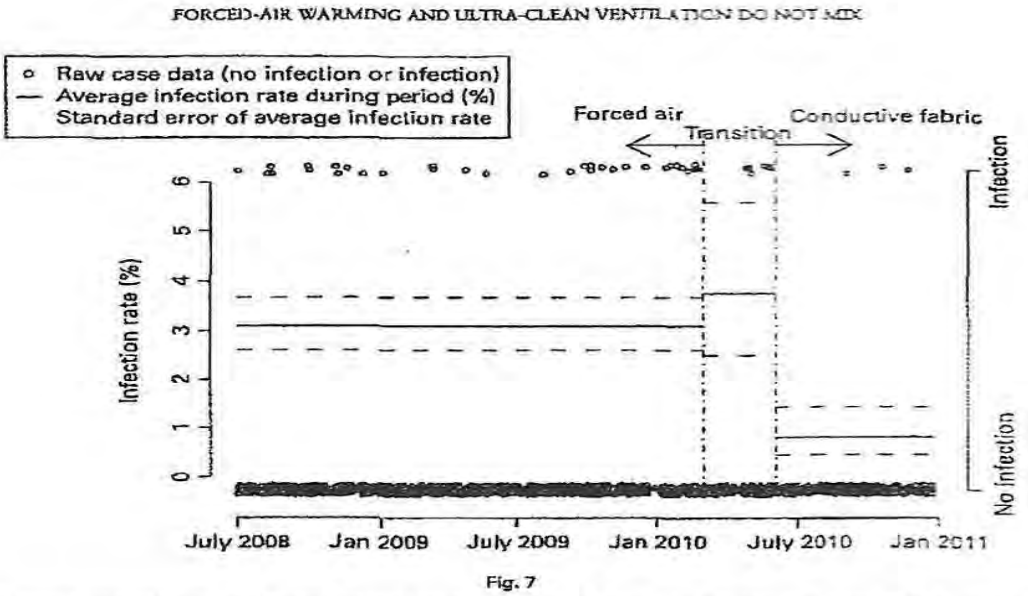


Fig. 7

Graph showing time-based trends of joint sepsis rates for hip and knee replacement cases. The outcome of each individual case is plotted on the right-hand axis (data are jittered to avoid overprinting). The infection rates for each period (forced-air, transition or conductive fabric) are plotted on the left-hand axis. Standard error of the mean was estimated using logistic regression.

Figure 11

A confusing finding is the more explicit but unpublished information on surgical infection rates over time, showing a progressive decline in rates over the first 8-12 months of the Bair Hugger period (Figure 12) followed by a later rise. If the Bair Hugger truly caused infection rates to rise, one would not expect a continue trend downwards as they were in use. The inconsistency is unexplained and suggests something else happened late in the Bair Hugger period to increase rates.

Further confusion related to the fall and later rise of rates in the Bair Hugger period relates to the fact that the authors had data for 9 months prior to the official study beginning. With the use of the Bair Hugger for these months, the infection rate was 0.68%, very low.

In contrast to the curve above (Figure 11) that was published – showing a flat line for infection rates during the Bair Hugger period, the true curve (Figure 12), showed an impressive decline with the Bair Hugger followed by a dramatic rise. One can only conclude that the latter was meant to obscure the raw data. It would have the effect of misleading the reader.

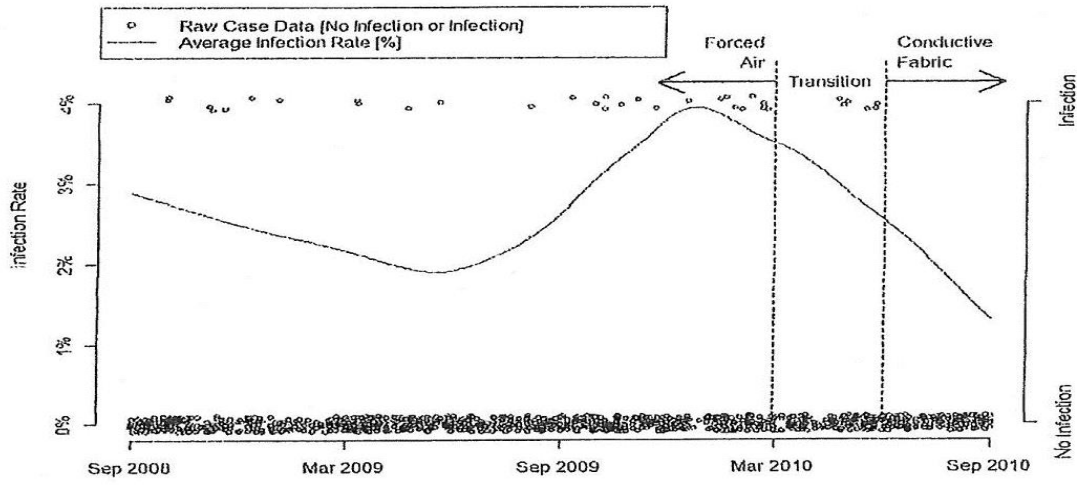


Figure 12

Figure 7: Infection data for n=1290 joint replacement cases with the outcome plotted on the right hand axis (data is jittered to avoid overprinting). A moving average of infection rate was plotted on the left hand axis. The change from forced air to conductive fabric patient warming in the orthopedic theaters is identified along with the transition period where both systems were used.

Given the unusually high rate of infection rate in the Bair Hugger era and the large proportion of *S. aureus* isolates recovered, some analysis by the hospital's infection control team a medical microbiologist or risk management office should have occurred. The microbiologist might have done finger printing of all *S. aureus* isolates to see if a single clone was dominant, indicating a common source problem. A review of OR procedures, perhaps some case control studies and interviews would all have been completed. The absence of such inquiries and analyses suggest a lapse in standard hospital safety.

The figure below shows the study design and highlights the known biases introduced over the 2-1/2 ear period of observation. (Figure 13 provided by Dr. Jonathan Borak)

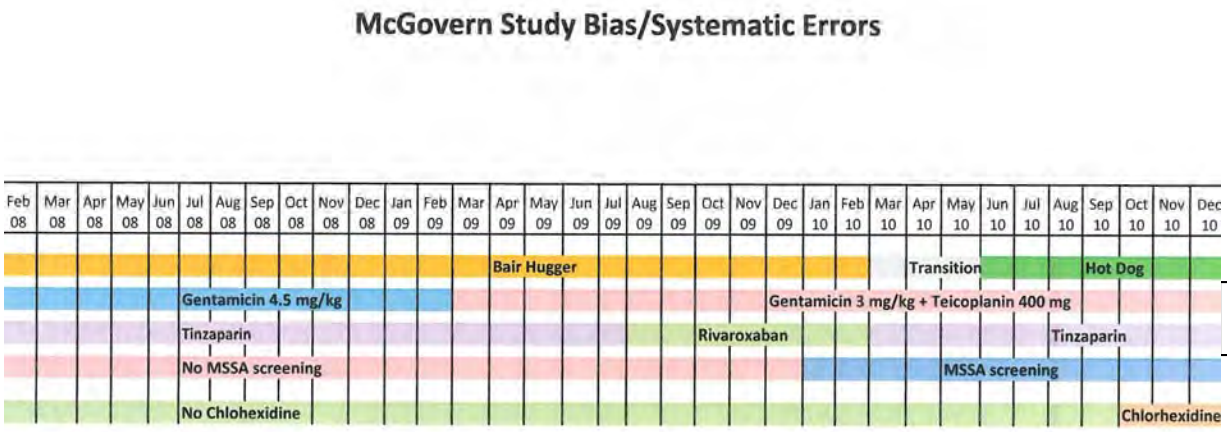


Figure 13

Some insight into a key change in standard patient management is provided by Dr. Mike Reed, consultant orthopedic surgeon at Northumbria Healthcare (*November 2011. The Clinical Services Journal. Infection Control in Orthopedic Surgery*). He stated in the article that he moved away from the traditional aqueous povidone – iodine skin prep to chlorhexidine alcohol. This change occurred in October 2010. That would favor a much lower rate of SSIs during that period late in the study. He also states that the "infection rate doubled when using gentamicin prophylaxis", the drug used exclusively during the Bair Hugger era. A possible cause for failure, prompting the change, was resistance to gentamicin by MRSA and coagulase negative staphylococci.

5) Further insights into the study flaws that failed to keep a level playing field were provided by Julie Gillson and Gail Lowden, who summarized the various protocol changes instituted by the Northumbria Healthcare NAS Foundation Trust (site of the McGovern study) which corresponded to reduced orthopedic SSI rates (5% to 0.9%) over time (The Clinical Services Journal. Ochler 2014. pp 71-74. See http://www.clinicalservicesjournal. Com/Handlers/FileHandler. Ashx? Fileld = 13230).

Such changes included – in 2008 – the identification of patients readmitted with an SSI; in early 2009, two full time SSI nurses were appointed to improve case finding and initiate "a robust and prospective surveillance; introduction of an SSI bundle in 2009, which included the introduction of octenisan antimicrobial skin washes preoperatively at home for all elective THR /TKR patients; subsequently OR disciplines were instituted limiting the number of people entering the OR area, no use of personal clogs, use of appropriate time of perioperative antibiotics and others. It is likely that hospital personnel became increasingly aware of the special focus on preventing orthopedic implant related infections. As a result, a "Hawthorne effect" would be in play, in which behavior changes occur among people who sense increased attention to their work activities. The Hawthorne effect is a form of confounding which can

improve work outcomes. Since the many protocol changes occurred late in the McGovern study, a Hawthorne effort for reduced infectious during the Hot Dog period would be expected. In the July 2012 issue of the Operating Theatre Journal, on (page 10) "Kimberly – Clark announces winners of inaugural HAI watchdog awards", championing infection prevention in UK hospitals:

"The winner of the category for operating theatre infection prevention initiative was Northumbria Healthcare NHS Foundation Trust which made a pledge to drive down surgical site infections (SSI) in Orthopedic Surgery."

They list the changes as employing two dedicated SSI surveillance nurses an a range of initiative in theatres including "restricting access to the department, screening patients for potential infections before they come into the hospital and improving skin preparation." They do not mention anything about use of the Hot Dog warming system.

In a crude subset analysis to provide insight into the observed effect during the Bair Hugger vs Hot Dog study periods, author and statistician Mr. Albrecht said that when rates of infection were confined to periods when the antibiotics and thromboprophylaxis drugs were the same, there was no significant differences ~ 1% for the Bair Hugger and 1% for the Hot Dog period (Albrecht deposition, pp 197-200).

Furthermore, when the infection rates were compared for the two devices (Bair Hugger vs Hot Dog), the rates were 4.3% for the rivaroxaban period vs 1.2% for the Tinzaparin period – when the antibiotics were held constant. The data illustrate the high risk of infection after rivaroxaban, a thromboprophylaxis drug never used in the Hog Dog period but on in the Bair Hugger period.

The McGovern study should be entirely discounted because of so many failures: it did not correct for numerous cofounders, was laced with several biases, and failed to establish a clear definition of case finding and show any independent validity of case finding methods to their recorded infection rates. The authors acknowledge that a causal relationship cannot be shown with this manuscript.

VIII. Investigating the Cause of a Cluster of Infections

A valid methodology exists to examine the cause of a cluster or epidemic of infections. When the rates of infection exceed a background threshold, a case control study is performed in which the exposures and experiences of infected cases are compared to appropriately matched uninfected controls. So the first step is to show statistically that the current rate exceeds background rates.

Once a difference in infection rates (baseline vs current) is found in exposures or experiences, statistics are applied to see if the differences are significant. Afterwards microbiological

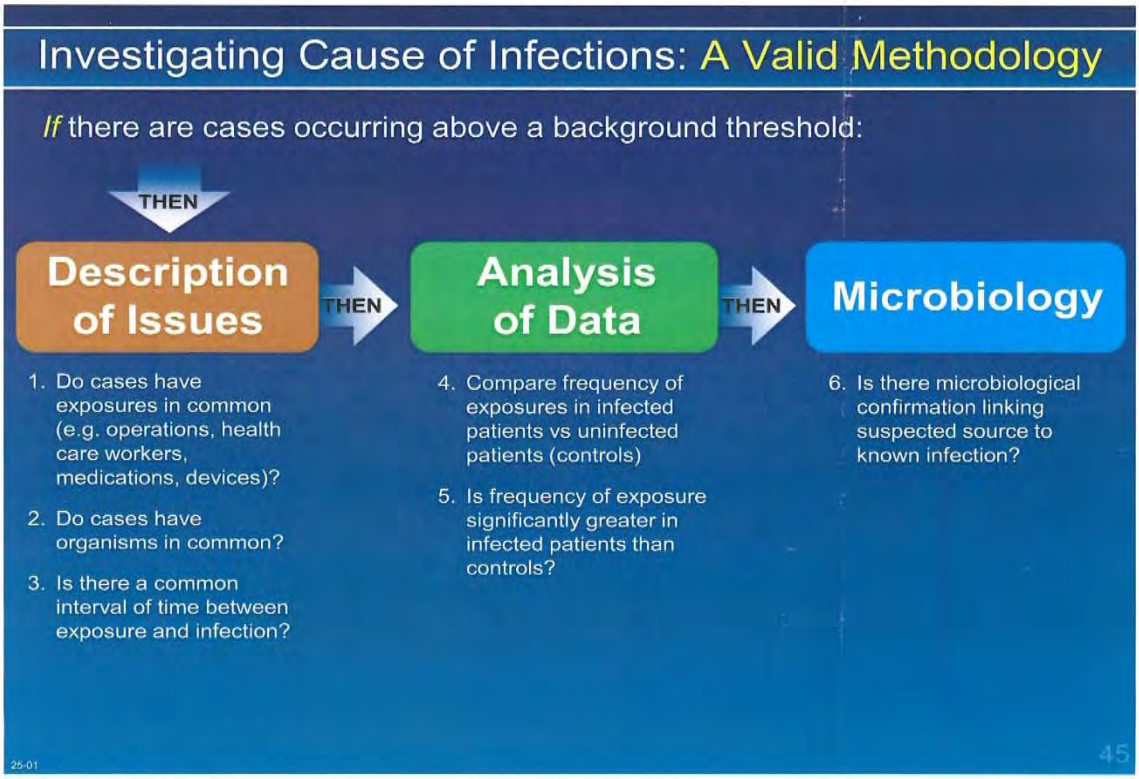


Figure 14

confirmation is sought to show that the exposure or experience was in some way linked to the same organism as encountered by the patient. (Figure 14).

If a single patient acquires an infection, in contrast to a cluster, there are limits to investigating the cause of that infection. Specifically, if the surgical site infection is not part of a cluster, if the bacterium implicated is commonly found on the microbiome, and if the investigation is not close in time to the date of surgery, then there is no significantly valid methodology to identify the source retrospectively. The most likely cause – the patient's own microbiome that was not adequately controlled – cannot be ruled out. The infected patients were most likely "pushed over the line" by their underlying risk factors.

Note that step 1 has never been shown – there are no regional, Statewide or National data to show a link between use of the Bair Hugger and a significant increase in SSIs. National trends corrected for confounders, show the opposite – a reduced rate of SSIs after THR and TKR during the Bair Hugger Era. The organisms implicated in infections are part of the microbiome of surgical patients. Infections afer surgery can often be explained by the underlying contribution of risk factors.

IX. Summary of the Report

A large number of patients who have undergone either a total knee replacement or total hip replacement have filed suit against 3M after they developed an infection of the prosthesis. The bacterial isolates identified in the many microbiology laboratories have varied, and no single organism with a unique fingerprint was demonstrated for all.

The patients with prosthetic joint infections live in several states in the U.S. and had surgery in many hospitals. Importantly, the plaintiffs have provided no data to show that an outbreak occurred at any hospital, in any state, or widely in the U.S. and traced the statistically elevated SSI rates to the Bair Hugger. Thus, they have not provided the first step in an investigation – show that an epidemic or unique cluster exists.

Those infected have alleged that the cause of their infection related to the use of peri-operative Forced Air Warming device called the Bair Hugger. Their hypothesis is that air currents in the operating room bring floor organisms up near the operative site, where they fall and incite the infection, and eventually lead to elevated infection rates.

The plaintiffs rely heavily on a single retrospective study by McGovern and colleges which purports to show an advantage of the Hot Dog resistance warming device to the forced air warming device – the Bair Hugger. The McGovern study team said in their publication that their data – showing fewer infections with the Hot Dog device - do "not establish a causal basis for this association." This is an appropriate statement, given the many flaws in study design, including a series of issues: Lack of case finding methods and validity, failure to control for numerous confounders, and introduction of several biases favoring the Hot Dog device. There is also the problem of a before – after design that did not allow for concurrent controls during the 2 ½ year study duration. Furthermore, one of the authors works for the competing company and thus has a significant conflict of interest.

In contrast, the Bair Hugger clinical trials utilized concurrent controls. Each study was prospective, with blind assessment of outcome and randomized. The two widely-cited clinical trials show statistically significant benefit for the Bair Hugger in reducing surgical site infections. These clinical trials are also supported by data from a meta-analysis, six cohort studies, an independent review by the ECRI institute, a case control study and U.S. national trends from the Centers for Disease Control and Prevention showing falling rates of infection in the Bair Hugger era after joint replacement. Furthermore, eight microbiological studies show no signal for harm from the Bair Hugger.

Current data suggest ~ 1% risk of infection after a THR or TKR with causative organisms that comprise the normal flora of the skin or nares, the microbiome of the skin or nasopharynx. Control of the microbiome – in the Bair Hugger era - has improved greatly in recent decades

due to the use of perioperative showers, nasal decolonization of *S. aureus,* improved skin antiseptic preps, warming, and others. Yet some patients still become infected. For the most part those infected are different from those not infected by virtue of comorbidities – conditions that increase the risk a priori for a SSI. These include obesity, diabetes mellitus, smoking, carriage of *S. aureus,* excessive alcohol intake and others. Current data support an altered microbiome in these comorbid medical conditions different from the normal microbiome.

The plaintiffs have presented eight manuscripts showing an increased temperature, particles or bubbles with the use of the Bair Hugger vs the Hot Dog, and showing some positive cultures of bacteria in use Bair Hugger devices. None indicate a relationship between Bair Hugger use and any infection. There might be viewed as hypotheses – generating studies, yet all true patient studies and microbiological data support the safety of the Bair Hugger. In the discovery phase of the trial, it has been shown that 7 studies showing safety of the Bair Hugger were not published, were kept secret.

An incontrovertible amount of data from the literature support the patient's own microbiome (flora of skin and nares) as key sources of the bacteria causing SSIs. Studies show that control of the microbiome by improved pre-surgical skin preps and use of effective nasal decolonization substantially reduce the SSI rate.

A debated question is how organisms get to the wound site from their microbiome reservoir on the skin and nares if the microbiome is not controlled. Possibilities include transient bacteremia after intubation; direct movement during surgery of the flora of the skin by instrumentation or hand carriage of the surgical team; some movement of the flora from the skin or nares to the air. Nasal carriage however is a marker of carriage elsewhere on the body. Organisms found in the nares are often found in the groin, perineum and axilla. The plaintiffs argue that the airborne route is key, citing the original studies by Lidwell and others. That study was flawed by not taking into account the use of antibiotics which had a higher effect (odds ratio) than the use of laminar air flow. Many hospitals introduced laminar air flow into operative suites after the Lidwell studies, however. The hypothesis is that SSI rates would fall and the reason they would fall was that the airborne bacterial load was reduced. However, four very large retrospective cohorts involving over 300,000 patients showed higher rates with LAF. A 2017 publication of a meta-analysis shows no benefit of LAF.

A recent study using a device to create a barrier to airborne bacteria did show a correlation but no cause effect could be established. So a question arises, does the Bair Huger influence the numbers of bacteria in the air of the operating room. A recent randomized study of air bacterial counts with the Bair Hugger vs the Hot Dog showed no influence of either warmer on the airborne number of bacteria.

I disagree strongly with the testimony of Dr. Jarvis, expert witness for the plaintiffs. In his deposition he correctly outlines the approach to an outbreak of infections (p.3) and concludes from his experience: "Our team's outbreak investigations established that culture surveys of personnel or the environment without a prior epidemiological investigation can be misdirected, expensive, or a waste of laboratory resources and therefore should not be performed before comparative epidemiological studies are completed. Our team's approach of integrating epidemiology and microbiology remains vital to conducting a successful outbreak investigation. The combined epidemiological – laboratory investigation approach has become the "gold standard" methodology…"

He then cites the correct epidemiological approach used in the Heater-Cooler outbreak due to *Mycobacterium chimaera*. Yet he ignores the fact that no such gold standard approach has been conducted to show that any outbreak exists with use of the Bair Hugger device: no increase in rates of SSI have been demonstrated as step 1 of a careful epidemiological investigation.

The plaintiffs have cited the clinical arm of the McGovern study as critical to their arguments. Yet Dr. Jarvis offers a superficial, single sentence mention (p. 12) that is uncritical and incomplete.

While focusing on pre-clinical studies of the Bair Hugger, Dr. Jarvis ignores a vast body of clinical studies showing the safety of the Bair Hugger: The second clinical trial (Melling), historical cohort studies, the case control study and national data infection rates in the era of the Bair Hugger.

His statement (p. 5) that "exogenous sources account for the majority of SSIs", is unreferenced and ignores the vast number of studies showing just the opposite – most are in fact endogenous.

Dr. Jarvis' deposition is superficial and wanting.

The overwhelming clinical data, national trends data during the Bair Hugger era and microbiological studies attest to the safety and benefits of the Bair Hugger.

I also disagree with Dr. Samet's testimony. His focus on the McGovern study is at face value and as a result is uncritical. His bias is illustrated by the gratuitous statement (p. 11) that concerns about confounding are "typical general claims made by those seeking alternative explanations for an association, and reach back to the strategies employed for decades by the tobacco industry".

Dr. Samet takes the univariate odds ratio of 3.8 in a flawed study at face value, stating that its size makes "confounding…unlikely… and not supported." He ignores the bias related to MSSA screening during the Hot Dog period and ignores the high numbers of *S. aureus* recovered in the Bair Hugger era and none found in the Hot Dog era after the initiating of MSSA screening in January 2010.

He fails to understand the bacteriological implication of a perioperative prophylaxis with gentamicin alone (Bair Hugger period) vs gentamicin plus teicoplasin. Dr. Samet did not address the bias in the use of no chlorohexidine alcohol skin prep during the Bair Hugger period vs the Hot Dog period during which time it was introduced. The many changes that occurred during the study essentially the SSI bundle – were also ignored by Dr. Samet, including case finding, preoperative skin cleansing, OR protocols, frequent team meetings and others.

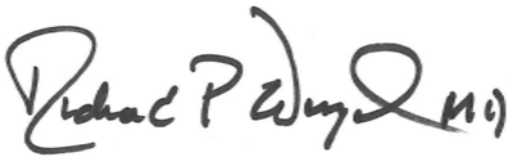
Dr. Samet's deposition is uncritical and wanting.

Of note, neither Dr. Jarvis nor Dr. Samet mentioned the five unpublished studies by Albrecht and others showing no bacteria observed in tests performed with the Bair Hugger device.

The overwhelming clinical data, national trends data during the Bair Hugger era and microbiological studies attest to the safety and benefits of the Bair Hugger.

To a reasonable degree of medical certainty, my opinion is that the Bair Hugger is not generally capable of causing a prosthetic joint infection. There is no valid scientific support for such a claim of any harm. Based on several lines of evidence, perioperative warming including warming with the Bair Hugger is a widely accepted infection control strategy.

Richard P. Wenzel, MD, MSc.



Date: 2 June 2017

Appendix:

Notes on Analogies of the Colonized Heater-Cooler Units

The plaintiffs allege that the Bair Hugger was analogous to the heater – cooler units, which have been linked to serious infections in patients after open heart surgery. The heater – cooler units used in cardiac surgery have been found to be contaminated with a single, very unusual organism – never before implicated in SSIs – *Mycobacterium chimaera*. This organism was not part of the normal patient microbiome and has been shown to have arrived on the apparatus from the manufacturer. An outbreak of *M. chimaera* infections has been demonstrated. No data support an outbreak of infections after use of the Bair Hugger. The species implicated are varied, and they are part of the microbiome of patients.

M. chimera is a slow-growing bacterium, a "distant cousin" of the organism causing tuberculosis. The infections typically are recognized many months after surgery. In part because mycobacteria divide slowly ~ every 24 hours. The reservoir (habitat) for *M. chimaera* is water. The organism was contaminated at the site of manufacturing before widespread distribution. The air from the HCU blows directly into the air in the operating room. The air in the Bair Hugger blows into the blanket and no one has shown that bacteria exit the blanket of the Bair Hugger.

The implicated heater –cooler units have a fan to cool the apparatus. The heater-cooler units have a large, open water tank, where the organism can be found. The fan directly blows onto the path of the surgical site, and *M. chimera* has been found in the air stream – the same species documented with a single fingerprint – as has been found on the machine and in patients. No airborne organism at the time of surgery with the Bair Hugger use has been linked to an organism found in the wound at surgery or subsequently in an infection, and recovered from the Bair Hugger.

Heater-cooler unit-related *M. chimaera* infections are totally different from those after use of Bair Hugger, which in fact has been shown to reduce infection rates.

Saxh et al. Prolonged outbreak of mycobacterium chimaera infection after open chest heart *Clin Infect Dis* 2015; 61:65-75. The author showed the same genus and species and fingerprint specimens from the water circuits of the heater, cooler unit and air samples when the device was in use, cardiac tissue specimens and blood cultures. This organism had previously never been known to cause post cardiac surgery infections, so a new epidemic was established.

Genetic analysis confirmed that many of the cases originated from source contamination at the Sorin 3T manufacturing plant. A spread within the hospital – a nosocomial link –was not established. Acherman Y et al. Prosthetic value endocarditis and bloodstream infection due to *mycobacteria chimera J Clin Micro* 2013; 51: 1769 – 73. Haller S et al. Contamination during production of heater – cooler units by mycobacterium chimera potential cause for invasive cardiovascular infections: results of an outbreak investigation in Germany. April 201 to February 2016. *Eurosurveillance* 2016:21.

Notes on Infecting Dose

For ethical reasons there are no studies showing the range of infecting doses of organisms that could cause an SSI after a joint replacement. For insight, the best data would come from animal studies of joint replacement – related infections.

Such models have been designed to create a reliable infection in a high proportion of animals to provide a reliable model of infections for study.

The models were not designed to identify the range of the infectious dose, but data from such animal models have been used to estimate the infecting dose.

Below are examples of some of the animal models used and the dose of organisms needed to cause infection. In each of these examples, *S. aureus* was the organism studied:

Notes on Animal Models – PJI-

Model/ref	No. Animals	Organism	Route of Infection	Inf Dose (cfu)
• English Short – Hair Rabbits Hip Durgery	125	*S. aureus*	IV	10^5
			Medullary Inoculation with prosthesis	<50
			Without prosthesis	10^4

Southwood
Br J bone Joint Sgy
1985; 67-B. 229-31

• New Zealand White Rabbits Knee Surgery Screw with polyethylene washer inserted	22	MRSA	Inject into knee	10^2, 10^3, 10^4 40% infection depending on dose; no change after 10^3

Craig
J Orthopedic Res
2005; 23:1100-1104

Model/ref	No. Animals	Organism	% Route Infection	Inf Dose
• New Zealand White Rabbits	10	*MRSA*	Injection into knee	10^5 - 10^8 cfu

Note: "With $5X10^4$ and $5X10^5$ cfu, only a few animals developed infection."
Belmatoug
J Infect Dis 1996; 174:414-7

• 12 week old mice Orthopedic k-wire placed into femur	Bioluminescent *S. aureus* injected into knee	$5x10^3$ or $5x10^4$ simulated acute infection; $5x10^2$ developed low grade infection, like a chronic infection

Bernthal **Note:** Some animals infected with only 500 cfus
Plos One 2010; 5: e 12580.doi:10.1371;

Journal.pone.0012580

Model	No. Animals	Organisms	Outcome
Sheep	10 5 -biofilm Infected 5 - No bacteria on film	MRSA	100% biofilm infected sheep became infected vs none of controls ~ 10 cfu/membrane

Williams DL
J Biomed Materials
Res 2010; 100: 1888-1900

Note: 1st model using biofilm organisms and not bacteria in solutions. The Goal was to simulate biofilm infection from a natural ecosystem contaminating a wound site after an open facture. MRSA, grown on a biofilm, was placed onto the tibia that had been stripped of periosteum and later covered with a stainless steel simulated fracture fixation plate.

Thus, the inherent flaws of animal models in predicting infectious doses in patients include the following:

1) No models use perioperative antibiotic prophylaxis, days of skin cleansing with antiseptic soap prior to surgery or use of topical nasal antibiotics to reduce the bioburden of the microbiome prior to surgery.

2) Almost all studies use virulent organisms, primarily *S. aureus* and not the relatively a virulent organism such as coagulase – negative staphylococcus or Gram negative rods. The infecting dose with less virulent organisms is likely to be greater than that with *S. aureus.*

3) The infecting methods in animal models include injecting bacteria directly into the prosthetic device or injecting a dose of bacteria directly into the bloodstream. Whereas the latter may simulate a perioperative bacteremia, the former does not happen in human surgery. Furthermore, no model has examined the airborne mode of infection.

It is generally thought that with a foreign body (joint prosthesis), the infecting dose of bacteria is less than that for surgery in which no foreign device is placed. The exact infecting dose range to infect 10% or 50% or more than 50% is unknown.

Addendum

- My CV and publications are attached as Exhibit A
- Materials used to inform my statements are listed in the body of my report. Others are attached as Exhibit B.
- My compensation is $600 per hour work and $700 per hour of testimony.
- I have not testified as an expert in the last four years.

RICHARD PUTNAM WENZEL
CURRICULUM VITAE

BIRTHPLACE Philadelphia, Pennsylvania

DEGREES

BS Haverford College, Haverford, Pennsylvania - 1957-61

MD Jefferson Medical College (Thomas Jefferson University) Philadelphia, Pennsylvania - 1961-65

MSc University of London, London School of Hygiene and Tropical Medicine (Epidemiology) London, England - 1985-86

SUMMARY OF CAREER

Date	Appointments	Institution
1965-66	Intern	Philadelphia General Hospital Philadelphia, Pennsylvania
1966-68	Residency, Internal Medicine	University of Maryland Hospital, Baltimore, Maryland
1968-69	Fellowship, Infectious Diseases	University of Maryland Hospital, Baltimore, Maryland
	Temporary assignment Dr. Robert Channock's Laboratory	National Institute of Allergy and Infectious Diseases National Institutes of Health Bethesda, Maryland
1969-70	Chief Resident, Internal Medicine	University of Maryland Hospital, Baltimore, Maryland
	Assistant in Medicine	University of Maryland Medical School, Baltimore, Maryland
1970-72	Lt. Commander, U.S. Navy Reserve Virology Division	Naval Medical Field Research Laboratory Camp Lejeune, North Carolina
1971-72	Consultant in Infectious Diseases	Department of Medicine U.S. Naval Hospital Camp Lejeune, North Carolina
1972-86	Hospital Epidemiologist	University of Virginia Medical Center, Charlottesville, Virginia
1972-76	Assistant Professor of Internal Medicine	University of Virginia School of Medicine Charlottesville, Virginia
1976-81	Associate Professor of Internal Medicine	University of Virginia School of Medicine Charlottesville, Virginia
1981-86	Founding Chair The Department of Epidemiology's Master of Science Degree Granting Program	Graduate School of Arts and Sciences, University of Virginia Charlottesville, Virginia

1981-86	Professor of Internal Medicine	University of Virginia School of Medicine Charlottesville, Virginia
1985-86	Senior International Fellow Fogarty Center National Institutes of Health	Department of Epidemiology London School of Hygiene and Tropical Medicine London, England
1986-95	Professor of Medicine and Preventive Medicine	The University of Iowa College of Medicine Iowa City, Iowa
1986-89	Director, Division of Clinical Epidemiology	The University of Iowa College of Medicine Iowa City, Iowa
1986-95	Director, Hospital Epidemiology and Statewide Epidemiology Services, Infection Control and Quality Assurance	The University of Iowa Hospitals and Clinics Iowa City, Iowa
1989-95	Director, Division of General Medicine, Clinical Epidemiology and Health Services Research	The University of Iowa College of Medicine Iowa City, Iowa
1993-95	Associate Chair Department of Internal Medicine	The University of Iowa College of Medicine Iowa City, Iowa
1995-2009	Professor and Chair Department of Internal Medicine	Virginia Commonwealth University Medical College of Virginia Richmond, Virginia
1997-8	Founder and Director of the Clinical Trials Institute	Virginia Commonwealth University
1997-2	Founder and Director of the VCU Outcomes Research Institute	Virginia Commonwealth University
2003-8	President, MCV Physicians The Practice Plan of the Health System	Virginia Commonwealth University
2005-8	Senior Associate Dean for Clinical Affairs	Virginia Commonwealth University School of Medicine
2010-2013	Professor and Former Chairman Eminent Scholar	Virginia Commonwealth University School of Medicine
2013 -	Professor Emeritus and Former Chairman	Virginia Commonwealth University School of Medicine

CERTIFICATION

American Board of Internal Medicine - 1971 #33226

Subspecialty, Infectious Disease - 1974 #33226
ACLS Certification 1985, 1997, 1999

MANAGEMENT EDUCATION

Date	Course	Institution
1986	Semester (1 hr/week) International Health Care	London School of Hygiene and Tropical Medicine University of London
1993	Health Care Finance	American College of Physician and Managerial Executives
1994	Marketing and Money: The Competitive Considerations	American College of Physician Executives
1994	Techniques of Financial Decision Making	American College of Physicians Executives
1995	The Future Role of Subspecialists in Departments of Internal Medicine	Association of Professors of Medicine
1996	Distribution of the Capitalist Dollar and the Redesign ofof Medicine Academic Health Centers	Association of Professors
1996	Market Evolution Continues - Strategies for Effective Change	University Health System Consortium
1996	Biomedical Research in Academic Departments of Internal Medicine	Association of Professors of Medicine
1997	Negotiation	Chester Karass Course
1998	Defining the Role of the Clinical Department Chair	AAMC
1999	Establishing Culture, Solving Problems, Mentoring	Association of Professors of Medicine

ADMINISTRATIVE ACTIVITIES

UNIVERSITY OF IOWA - 1986-1995

Associate Chair
Department of Internal Medicine

The main responsibilities are for the development of new programs and review of existing policies. Such issues as development of Primary Care initiatives for Internal Medicine, the articulation of a policy for managing substance abuse in employees, and the review of all committees are recent activities.

Director
Division of General Medicine, Clinical Epidemiology and Health Services Research

The main responsibilities were traditional activities in an academic medical center with oversight for teaching, research and clinical activities. There were 26 members of the faculty (5 dual appointments) and 11 fellows for 1994-95. There were also five clinical study nurses, two laboratory

technologists, a half-time statistician, two managing editors, several MS and PhD students and several part-time students who work with the Division. The Division Director had oversight of the General Medicine Clinic (Clinic B) through which all medical residents rotate and who are supervised in each session by 2-4 faculty members from the Department of Internal Medicine. Each year the division director organized a two-day Clinical Epidemiology Symposium which has attracted nationally recognized speakers in wide areas of expertise.

The Division Director was PI of the only NIH-supported training grant for Hospital Epidemiology. Recruiting was done on a national level.

Director
Hospital Epidemiology and Statewide Epidemiology Services, Infection Control and Quality Assurance

Oversee the Hospitals Epidemiology and QA Program (41 personnel plus part-time employees), the surveillance and analysis systems and outreach investigation. Consultation by phone was provided for all hospitals in the state, and two courses each yeartwo weeks eachwas provided. Our laboratory, shared with the Department of Pathology, performed molecular typing of organisms.

Director
Preventive Medicine Graduate Course

1) Epidemiology of Infections (4 hours), and
2) Epidemiology of Nosocomial Infections (3 hours)

These courses were given on alternate winter schedules - 1 to 2 times weekly January to May. Approximately 20-30 graduate students are enrolled for each course.

MEDICAL COLLEGE OF VIRGINIA/VIRGINIA COMMONWEALTH UNIVERSITY - 1995-

Professor and Former Chair
Department of Internal Medicine (2009 – Current)

Chair
Department of Internal Medicine (1995-2009)

The responsibilities are to maintain and enhance the teaching, research, and service mission of the Department and maintain financial stability. There are 200 full time faculty members in the Department and an annual operating budget of $50 million. The research budget is $26 million. Contract budgets are approximately $18 million.

President
Financial and Operations Board of Internal Medicine (1995- 2009)

The Financial and Operations Board reviews Departmental finances monthly, every request for new recruiting and hires, and issues related to clinical operations.

Director
Institute for Outcomes Research, VCU (1997-2002)

The President of VCU has designated $250,000 per year for operating expenses of the newly designated Institute. The director is responsible for its growth in research, oversight of administrative and biostatistical support staff. By mid-2000, the Institute was handling $10 million in research contracts. The Institutes for Clinical Trials and Outcomes Research were re-organized under the V.P for Research office in 2002 with a large expansion of activities.

President
MCV Physicians (2003-8)

This is the first elected president since the foundation of the VCU Health System. The clinical chairs elected the President without term to oversee the

$160 million budget.

Senior Associate Dean for Clinical Affairs (2005- 8)
This position was created to link the Practice Plan with the School of Medicine (office of the Dean)

NATIONAL ACTIVITIES

U.S. Congress

1979-80 Consultant to U.S. House of Representatives Ethics Advisory Board on Ethics Regarding Freedom of Information and Infection Surveillance Data, Washington, D.C.

National Institutes of Health

1987-88 Special Consultant, National Institutes of Health Study Section: Epidemiology and Disease Control (#2)

1988 Consultant, Small Business Innovation Research Phase I Contract Proposals for the National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health

1988-92 Member, National Institutes of Health Study Section: Epidemiology and Disease Control (#2)

1995 Member, Special Committee of the Microbial Physiology and Genetics - 2 study section

1997-2000 Member, Microbiology and Infectious Diseases Research Committee of NIAID

1997 Consultant: Emergence of Drug Resistance in *Staphylococcus aureus*

2000-06 Affiliate member NIAID Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) program

Infectious Diseases Society of America

1988-91 Council Member (elected), Infectious Diseases Society of America (IDSA)

1988-91 Member, Publication Committee, Infectious Diseases Society of America (IDSA)

1990-91 Member, Subcommittee on Advertising of the Publications Committee, Infectious Diseases Society of America (IDSA)

1993-95 Chair, Task Force on Outcomes Research, Infectious Diseases Society of America (IDSA)

2002-05 Member, Annual Program Committee

International Society for Infectious Diseases:

2000-04 Executive Board Member
Chair, Infection Control Working Group

2004-06 **President-elect**

2006-08 **President**

2009 – 2014 **Executive Board Member**

Veterans Affairs

1990 Consultant, National VA Multicenter Study on the Efficacy of AZT in Delaying Onset of AIDS in HIV Infected Patients With

	CD4 Counts Less Than 500 and Greater Than 200
2004-	Member, National Research Advisory Council for Veterans Administration.
2008-	NRAC Subcommittee on OIF/OEF Va Research portfolio
2008-	**Chairman, National Research Advisory Council for Veterans Administration 2008-2013**
2011	Member – Gulf War Steering Committee
	Institute of Medicine/National Academies
1991	Institute of Medicine Task Force on the National Threat from Bacteria, Rickettsia, and Chlamydia
2001	Invitation-only meeting "Balancing National Security and Open Scientific Communication: Implications of September 11th for the Research University"
2010	Member, IOM Committee on Personal Protective Equipment for Healthcare Workers to Prevent Transmission of Pandemic Influenza or Other Viral Respiratory Infections:Current Research Issues
	Antimicrobial Agents and Chemotherapy of the American Society for Microbiology
1984-87	Program Committee, Interscience Conference on Antimicrobial Agents and Chemotherapy, American Society of Microbiology
1987	Young Investigator Awards Subcommittee for the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC)
	American Medical Association
1991-92	American Medical Association, Infection Control Certification Project Planning Group
	Association of Professors of Medicine
1995-	Member
2004-	APM Finance Committee Member
	Centers for Disease Control and Prevention
1979-80	Member, Scientific Steering Committee for the Second International Symposium on Nosocomial Infections sponsored by the Centers for Disease Control, Atlanta, Georgia
1993	Consultant, Centers for Disease Control Advisory Committee on Prevention of HIV Infection; Subcommittee to review the HIV prevention strategy: “Monitoring the HIV/AIDS Epidemic” Hospitals
2004	Member, Healthcare Infection Control. Advisory Committee - Surveillance Group Management.
	International Conferences
1983	Scientific Program Chair, First International Symposium on Infection Control, April-May, Vienna, Austria
1985-86	Scientific Program Chair, Second International Symposium on Infection Control, London, England (Meeting cancelled)

1986-87	International Advisory Panel, 1987 meeting of the Hospital Infection Society, Great Britain
1988	International Board, International Symposium on Nosocomial Pneumonia, September 1-2, 1988, Freiburg, West Germany
1988-90	International Advisory Board, Second International Meeting on Bacterial Epidemiological Markers, April 9-11, 1990, Rhodes
1988-90	International Advisory Panel, 1990 meeting of the Hospital Infection Society, Great Britain
1989-90	Scientific Committee, 1st International Conference on the Prevention of Infection, Nice, France
1991	International Scientific Board for the International Symposium on Nosocomial Infections Due to Intravenous Devices, June 21-22, Freiburg, Germany
1992	International Board - Fifth Meeting of the Spanish Society for Infectious Diseases and Clinical Microbiology, November 10-13, 1992, Barcelona, Spain

INTERNATIONAL ACTIVITIES

Pan American Health Organization

1984	Consultant, Pan American Health Organization, National Meeting. Trained leaders in Hospital Infection Control, March. Brazilia, Brazil

International Field Trips

1964	Cholera field trip with the U.S. Navy Medical Research Unit II to Manila, Philippines under Robert A. Phillips, Capt. USN, sponsored by Dr. Kenneth Goodner, Chair, Department of Microbiology, Jefferson Medical School. Recipient of the "Order of the Perforated Pad" for Cholera field work lasting over 35 days.
1967	Cholera field trip, Dacca and Malumghat, East Pakistan with the Pakistan SEATO Cholera Research Laboratory, October through December. Director, Robert A. Phillips, M.D.

Pan American Health Organization

1982	Consultant, Pan American Health Organization, South American International Meeting. Training of Teachers in Hospital Infection Control, September 11-17 and November 27- December 7, Santiago, Chile

World Health Organization

1984-	WHO Expert Advisory Panel, Acute Bacterial Diseases

Other

1965-	Class representative for the Alumni of Jefferson Medical College
1968-69	President of House Staff Association of Interns, Residents and Fellows, University of Maryland Hospital
1974-77	Member, Ad Hoc Advisory Panel of the National Coordinating Committee on Large Volume Parenterals.
1987-89	Program Committee, Surgical Infection Society
1987	Infection Control consultant to the University of California Systemwide Task Force on AIDS
1988-89	Co-Chair, Scientific Program Committee for the Baltimore, MD, March 1989 meeting sponsored by the Society of Hospital Epidemiologists of America (SHEA) and the journal Infection

Control and Hospital Epidemiology

1994 Public Policy Committee for the Society of Hospital Epidemiology of America, Inc.

2002 -2004 Academic Advisory Board for the Visiting Professorship in Infectious Diseases - Pfizer, Inc.

MEDICAL CENTER ACTIVITIES

UNIVERSITY OF VIRGINIA

1972-85 Infection Control Committee, University of Virginia Hospital

1976-79 DNA-Recombinant Committee, University of Virginia

1979-80 Professional Standards Review Organization, (P.S.R.O.), University of Virginia Hospital

1979-81 Medical Care Evaluation Committee, University of Virginia

1979-85 Biohazards Committee, University of Virginia

1979-85 Pharmacy and Therapeutics Committee, University of Virginia

1980-82 Audit and Quality Assurance Committee, University of Virginia Hospital

1981 Intern Selection Committee, Department of Medicine, University of Virginia

1981-82 Member, Shenandoah Professional Standards Review Foundation Medical Care Evaluation Committee

1981-82 Chair, Shenandoah Professional Standards Review Foundation Medical Care Evaluation Committee

1984 Executive Committee, Council on Medical Education, University of Virginia

1984 Southeastern Cancer Study Group
Chair, Preventive Oncology Subcommittee, Cancer Committee, University of Virginia

1984-85 Council on Medical Education, University of Virginia

1984-85 Member, Alumni Consultants Council
University of Virginia Medical School Alumni

1984-85 Cost Control Committee, University of Virginia

UNIVERSITY OF IOWA

1986-95 Chair, Infection Control Subcommittee, University Hospitals and Clinics Advisory Committee, University of Iowa

1987 Promotions Committee, evaluation of Associates, Instructors, and Assistant Professors, Department of Internal Medicine.

1987 Promotions Committee, evaluation of Associate Professors, Department of Internal Medicine, University of Iowa

1987-93 Hospital Information System Advisory Subcommittee, University Hospitals and Clinics Advisory Committee University of Iowa

1987-89	Residency Selection Committee, Department of Internal Medicine, University of Iowa
1987-90	Chair, Subcommittee for Quality Assurance of Professional Practice Committee, Department of Medicine, University of Iowa
1987-90	Chair, Search Committee for Director of Division of Clinical Pharmacology, Department of Internal Medicine University of Iowa
1988	Chair, Promotions Committee, Evaluation of Associate Professors, Department of Internal Medicine, University of Iowa
1988-89	College of Medicine Lecture Committee, University of Iowa College of Medicine
1988-89	Co-PI at University Hospitals and Clinics for RAND Corporation Sponsored Academic Medical Centers Consortium for Quality and Appropriateness of Care, University of Iowa

ACTIVITIES

1989-90	Member, Search Committee for Head of the Epidemiology Division of the Department of Preventive Medicine, University of Iowa College of Medicine
1989-95	Member, Department of Internal Medicine Clinical Research Task Force, University of Iowa College of Medicine
1989-95	Member, University-Wide Task Force on Infectious Diseases, University of Iowa
1989-95	Editor, *EPI-GRAM*, quarterly bulletin published statewide in Iowa and focused on quality assurance and hospital epidemiology issues, University of Iowa Hospitals and Clinics
1989-91	Director, 4th Year Medical Student Course, "Clinical Pharmacology and Therapeutics," University of Iowa College of Medicine
1990-95	Ethics Advisory Committee, University of Iowa College of Medicine
1990-91	Chair, Ad Hoc Committee to review Program of Hospital and Health Administration and select next program head
1990	Member, University Task Force to design the Center for Health Services Research and Policy Analysis
1990-95	Director, Graduate Course in Prevent Medicine, "Hospital Epidemiology"
1991-92	Member, Geriatrics Task Force
1991-92	Member, Committee to review adjunct faculty (PhDs) for membership on faculty of the Department of Internal Medicine
1991-95	Director, Graduate Course in Preventive Medicine, "Epidemiology of Infectious Diseases"
1991-96	Principle Investigator and Director of the National Institutes of Health-Sponsored Fellowship Program in Hospital Epidemiology

1992	Chair, University President's Committee to select the newly designated Vice-President for Health Sciences
1993	Associate Chair, Department of Internal Medicine
1993	Member, Biotechnology Drug Advisory Subcommittee of the Hospital Advisory Committee
1993	Chair, Committee on Committees, Department of Internal Medicine
1993	Chair, University Industry Conflict of Interest Committee, Department of Internal Medicine
1993	Member, Center for International Rural and Environmental Health
1994	Collegiate Self-Study Subcommittee for Basic Sciences Department
1994	Committee to Review Full Professors, Program of Hospital and Health Administration
1994	Joint Strategic Planning Committee, The University of Iowa Office of The Vice President for Health Sciences and The Executive Office of Mercy Hospital
1994	Department of Medicine Committee to Organize and Implement Preparations for a Multi-Purpose Arthritis Center Proposal
1994	University Committee for Education Trainee Issues
1994-95	Search Committee for University Hygiene Laboratory Director
1995	Chair, Vice President for Medical Science Feasibility Study Committee to consider establishing a school of public health and allied health
1995	Task Force on Managing Health for Subcommittee on UIHC Strategic Planning
1995	Chair, Committee to Review Division of Cardiology, Department of Internal Medicine

MEDICAL COLLEGE OF VIRGINIA OF VIRGINIA COMMONWEALTH UNIVERSITY UNIVERSITY

1995-7	Chair, General Clinical Research Center (GCRC) Advisory Board
1995-	Board Member, MCV Associated Physicians
1995-	Chairman, Clinical Practice Committee of the MCV Associated Physicians
1995-96	Chair, Search Committee for Division Chair of General Medicine, in the Department of Internal Medicine
1995-	GME Allocations Committee
1995-96	Search Committee for Director of Massey Cancer Center
1995-	Chairmans Advisory Board to MCV Hospital
1995-	Executive Committee of the Faculty

1995-	Executive Committee of the MCVH Medical Staff
1995-	Executive Council of the Generalist Initiative
1995-	VACGM Executive Committee
1996-00	Member, MCVAP Managed Care Committee
1996-9	Curriculum Change Stearing Committee
1996- 97	Chair, Search Committee for Chair of Radiology
1997-	Member, Faculty Recruitment Review Committee, School of Medicine
1997- 2014	Member, Advisory Committee for the V.P. for Strategic Planning
1997-2001	VP for Health Services Advisory Committee to the office of Health Policy and Research
1997- 2014	Member, Senior Committee for Senior VP/COO for MCV Hospitals
1998- 2014	MCV Hospital Authority Board
1999- 2014	MCV Hospital Authority Board Subcommittee on Quality, Safety and Credentials
1999-	**Member of the MCV Foundation Board of Directors**
1999-	Trustee. MCV Foundation
2000- 2002	Strategic Planning Committee of the VCU's Health System Board
2001-2	Chair, Search Committee for the Chair of Ophthalmology
2001-	Member, University Health System Task Force on Finances and Human Resources
2002 - 2006	Member, Research Advisory Council for VCU
2002-3	Member, Search Committee for the Chair of Surgery
2003- 4	Member, Search Committee for CEO of MCVH
2003- 9	Member, MCV Physicians Board
2003-10	Member, VCU School of Nursing Advancement Council
2005- 9	Chair, Dean's Committee for Strategic Development of Translational Research at VCU

PROFESSIONAL SOCIETIES

Association of American Physicians
American Society for Clinical Investigation
American Clinical and Climatological Association
Association of Professors of Medicine
Infectious Diseases Society of America (**Fellow**)
Council Member (elected) - 1988-1991
Member, IDSA Society Awards Committee – 2007-10
American Epidemiological Society
American College of Epidemiology (**Fellow**)
Southern Society for Clinical Investigation - through 1986

Central Society for Clinical Investigation - 1987- 95
American Federation for Clinical Research
American College of Physicians (**Master**)
American Society for Microbiology
Association for Practitioners in Infection Control
Surgical Infection Society (**Charter Member**)
Society for Epidemiologic Research
Hospital Infections Society (Europe)
International Epidemiological Association
International Society for Infectious Diseases **President-elect** - 2004 - 2006
President - 2006-2008
Executive Board Member – 2009 - Current
American Academy of Microbiology (**Fellow**)

PROFESSIONAL SOCIETIES

Society of Hospital Epidemiologists of America
Vice President - 1983
President Elect - 1984
President – 1985
National Research Advisory Council of the Veterans Affairs. Member 2005-
Chair: 2008-2012
Albemarle County Medical Society - 1972-1986
Medical Society of Virginia - 1972-1986
Royal Society of Medicine (Affiliate)
Sydenham Society

AWARDS

1971 **Sir Henry S. Wellcome Medal and Prize for 1971**
The paper was entitled, "Acute Respiratory Disease: Clinical and Epidemiologic Observations of Military Trainees" (Presented December 7, 1971 at the Annual Convention of Military Surgeons). The award consisted of a silver medal, scroll and honorarium. It was established by Sir Henry S. Wellcome in 1916 and is awarded annually by the Association of Military Surgeons of the United States. The award is sponsored by the trustees of the will of the late Sir Henry S. Wellcome L.L.D. F.R.S. for the best essay on a subject of the author's choosing that relates to military medicine.

1974 **Major Louis Livingston Seaman Prize**
For notable article published in Military Medicine, presented in San Diego, California October 28, 1974 at the Association of Military Surgeons. The article was entitled "Malaria in Vietnam (I Corps Sector): Review of 214 cases including EEG patterns of 19 acutely ill patients."

1978 **Annual award of the Virginia Association of Practitioners of Infection Control** for Contributions to APIC, Virginia

1985-86 **Senior International Fellowship- NIH**
Fogarty Center of National Institutes of Health for work per formed at the London School of Hygiene and Tropical Medicine

1990 **Burlington Northern Foundation Faculty Achievement Award**
For excellence in teaching. This is an annual award given by The University of Iowa Council on Teaching for outstanding teaching, scholarship, and service over a career.

1994 A**bbott Achievement Award for Outcomes Research**
Infectious Diseases Society of America. The $50,000 award is designed to support the work of an individual initiating a project to advance a cause important to infectious disease physicians

and to the Society.

1994 **Regents Award for Faculty Excellence**
This award is given annually to a member of the University for excellence in service, research, and teaching, specifically for a "sustained record of excellence across the spectrum of faculty endeavors."

1994-96 **Humboldt Research Award for Senior U.S. Scientists**
Granted in recognition of past accomplishments in research and teaching. These research awards--$65,000--including invitations to undertake prolonged periods of research in the Federal Republic of Germany - are intended to promote long-term specialized cooperation between foreign and German researchers and their institutes.

1997 **Woodward Award and Lecture**
U.S. Navy Occupational Health and Prevention Annual Workshop
This award included a lecture to 2,100 delegates given to recognize "vision and leadership in Public Health and Preventive Medicine."

1997 **Society for Healthcare Epidemiology (SHEA) Annual Lecturer and Award**
In recognition of extraordinary career contribution to Infection Control and Healthcare Epidemiology. St. Louis, April

1999 **James D. Bruce Memorial Award**
Presented by the American College of Physicians - American Society of Internal Medicine for "distinguished contribution in Preventive Medicine"

1999 **Thomas E. O'Brien, MD Memorial Lecture Award for Excellence in Medicine**. In recognition of outstanding lifetime achievements in the field of Medicine. INOVA/Fairfax Health System 14 November 1999

2001-2 **Contemporary Clinical Medicine "Great Teacher"** - named by the **National Institutes of Health;** Special Lecture - 14 Nov 2001.

2002 Awarded **Mastership** of the American College of Medicine

2002 **University of Iowa Distinguished Achievement Award** from the Department of Internal Medicine. Presented to former or current faculty every two years, the award is given to an extraordinary scientist and mentor.

2003 Jefferson Medical College's **Distinguished Alumni Award**. This is an annual award given to an alumnus and the highest accolade given by the Alumni.

2004 **W. Robert Irby Award**, for *Leadership in Philanthropy*, presented by the MCV Foundation. July 9th.

2008 **Laureate Award**, American College of Physicians – Virginia Chapter – for an abiding commitment to excellence in medical care, education or research and In service to their community, their Chapter and the American College of Physicians.

2008 **Pioneer in Medicine Award** – Voted on by physicians in the Greater Richmond area and featured in *Richmond Magazine*.

2009 **Educational Innovation Award** of the VCU School of Medicine. The Award recognizes the VCU theatre-medical project.

2010 Elected **Honorary Member of the Mexican National Academy of Medicine** for lifetime achievements and help for the citizens of Mexico.

2010	**Maxwell Finland Award for Scientific Achievement** from the National Foundation for Infectious Diseases. Criteria for the Award include excellence in clinical/Research activities; participation in training future leaders; and positive impact on the health of humankind.
2010	**Faculty Achievement Award at VCU**: The Hightest Award Given at the University
2010	**Edward Kass Award and Lecture** - National Meeting of the Infectious Diseases Society of America, for a distinguished career in infectious diseases. Vancouver.
2011	**Elaine Larson** Lectureship and Award – National Meeting and the Association of Practitioners of Infection Control for lifetime achievement. Baltimore
2011	**Elaine Larson Award and Plenary Lecture** Association of Practitioners of Infection Control. Baltimore
2012	**McGovern Compleat Physician Award** – Presented by the Houston Academy of Medicine (January). The John P. McGovern Compleat Physician Award, established in 1993, is presented annually by the Houston Academy of Medicine to recognize a physician whose career has been founded on Oslerian ideals of medical excellence, humane and ethical care, commitment to medical humanities and writing, research, and harmony between the academician and medical practitioner. These characteristics were exemplified by the life of Sir William Osler, who is revered world-wide as the "Father of Modern American Medicine."
2013	**2013 SHEA Mentor Scholar Award** to honor individuals who are recognized for their dedication and excellence in mentoring trainees in infection prevention and control SHEA is the society for healthcare epidemiology of America.
2014	**2014 Martin Favaro Award** from the International Federation for Infection Control for Lifetime Achievement.
2014	**Presidential Medallion -** An award from VCU presented for his contributions, talent, leadership, and vision.
2015	**Simon Gratz Award** – Jefferson Medical College for significant medical research initiatives.

HONORS

1981	National Foundation of Infectious Diseases Lecturer at the Annual Meeting of the National Association of Practitioners of Infection Control, Atlanta, Georgia, May 18, 1981
1983	Elected as honorary member of AOA by the AOA student members of Alpha Chapter at the University of Virginia Medical School
1985	Invited lecturer, National meeting of the Infectious Diseases Society of America: "Evolving Art and Science of Hospital Epidemiology," Minneapolis, Minnesota, October 1985
1986	Invited keynote lecturer, National meeting of the Swedish Society of Sterilization and Infection Control: "Surveillance of Hospital Acquired Infections," Göteborg, Sweden, June 1986
1988	Invited keynote address, Annual Meeting of the Association for Practitioners in Infection Control: "Interaction of Man and Microbe: Implications of the AIDS Epidemic for Hospital Epidemiology," Dallas, Texas, May 1988
1989	Invited lecturer - Division L - Annual Address National Meeting of the American Society for Microbiology, New Orleans, May 9-14, 1989

1991	Keynote speaker, National Meeting of the Hospital Hygiene Society, Norway
1991-00	Listed in The Best Doctors in America, Woodward/White Inc.
1993	Special Honor of the Society of Hospital Epidemiology for editorship of *Infection Control and Hospital Epidemiology*, 1980-1993
1995	Listed in Sterling *Who's Who* Directory
1997	Life Member of the National Registry of Who's Who
1997-	Honorary Membership of the Mexican Society for the Study of Nosocomial Infections Presented in Mexico City
1999-	53d Shelton B. Horsley lecturer – Richmond Academy of Medicine
2001	**Nominee - "Best Teacher"**. One of five finalists voted by the 4th year medical students at the Medical College of Virginia
2002	Annual Walter Reed Lecture - Richmond Academy of Medicine: "The History of Biological Terror." May 8th.
2002	**Nominee - "Best Attending."** One of nine finalists voted by the 4th year medical students at the Medical College of Virginia.
2002	**Nominee - Outstanding Teaching Award.** One of nine finalists voted by the 4th year medical students for this separate award at MCV
2004	Speaker - Annual Great Pearls Day for graduating M-4s at MCV (one of seven faculty members selected)
2005	Keynote speaker, National Meeting for Infection Control, New Zealand.
2005	**The Excellence in Teaching Award** by the VCU Internal Medicine Housestaff for committment to the ideals of education, research, and clinical service. 19 May
2005	Invited speaker (one of seven worldwide) to the Symposium, celebrating **the 100th Anniversary of the Nobel Prize for Robert Koch**. Sponsored by the Robert Koch Institute. Berlin, 28 October.
2005	Elected Trustee of the Richmond Academy of Medicine.
2007	Finalist, Outstanding Faculty Award presented by the Commonwealth of Virginia State Council of Higher Education.
2007	Hooder at MCV Graduation – One of two faculty members voted by the 4th year Medical School class
2008	Outstanding Teacher Award (from students) M-III Medicine Clerkship
2008	The Most Skilled CPC Diagnostician teaching award from the Internal Medicine Housestaff
2009	The Moss Lectureship Award by the Virginia Chapter of the ACPit is the opening plenary talk "The Least Lecture"
2009	University of Virginia. Dr. William Parson's Visiting Professorship. The most important visiting professorship in Internal Medicine at the UVA

	2009	Oregon Health Science Center. H.P. Lewis Visiting Professorship, the most important visiting professorship at the Oregon HSC
	2009	**Commencement Speaker** VCU Graduation for Master and PhD graduates in the Department of Epidemiology
	2011	**Commencement Speaker** chosen by the VCU graduates – School of Medicine
	2011	**Keynote Speaker** Annual Meeting of APIC (4100 in attendance) APIC is The Association for Preventionists in Infection Control, Baltimore, MD
	2013	One of the 12 panelists in the 40th APIC Annual Meeting Keynote Presentations (4500 in attendance) Ft. Lauderdale, FL
	2014	Faculty excellence in teaching award from the VCU housestaff
	2014	Keynote speaker annual senior student forum for research. Emory University, Atlanta Georgia
	2016	James Moss Lecture: The art and science of physical diagnosis. Virginia ACP Chapter Meeting - March
SPECIAL/NAMED VISITING PROFESSORSHIPS	1982	Visiting Professor, Chang Gung Memorial Hospital, June 1- 30, Taipei, Taiwan
	1991	E.B. Flink Visiting Professor, The University of West Virginia, April 8-10
	1992	Richard Bowman Lectureship and Visiting Professor, The University of Virginia, Charlottesville, Virginia, October 8-11
	1993	Dr. Maurice C. Pincoffs Lecturer in Medicine, The University of Maryland School of Medicine, December 6
	1994	University of Geneva, Geneva Switzerland, March 20-25
	1994-1997	Institute of Hygiene and Microbiology and University of Cologne, Germany, July 1-30
	1994	Edmond Lowbury Lectureship - Opening lecture of the Hospital Infections Society (United Kingdom) presented at the triennial meeting of the Society in London, September 1994
	1996	Dascomb Lecturer, Louisana State Univerisity School of Medicine, New Orleans, October 24-25.
	1999-	Memorial Lecturer. Fairfax/Inova Hospital, Fairfax, Virginia
	1999	Pfizer Visiting Scholar - Stanford University School of Medicine
	2000	Visiting professor. Harvard Medical School. May 31- June 1
	2001	Visiting Professor. Johns Hopkins University School of Medicine. January 24-26
	2001	The Sonia Stupniker Isard Lecturer for the College of Physicians of Philadelphia - "Biological Terror". December 6, 2001.
	2003	James Hammarsten visiting professor and lectureship, University of Oklahoma, March 4-5.

	2003	Franklin Koontz visiting professorship and lecturer, University of Iowa College of Medicine, May 7-9.
	2004	Robert J Fass Award and Visiting Professorship. Ohio State University, June 2-3.
	2008	Summer Memorial Trust Lecturer. Oregon Health Sciences University and Providence St. Vincent Medical Center 10-11 May
	2008	Watanakunakorn Lecturer. Northeast Ohio University of Medicine; 29 September
	2009	Howard P. Lewis Visiting Professorship – The University's Most Distinguished Professorship. Oregon Health Sciences University, Portland, Oregon. 2-6 November
	2013	Visiting Professor – University of Cologne, May 2013
	2013	Visiting Professor – University of Basel, October
	2016	Benson – Kendell Visiting Professorship Oregon Health and Science University, Portland, Oregon
	2016	Visiting Professor – University of South Carolina
JOURNAL EDITORSHIP	1979-93	**Founding Editor**, *Infection Control and Hospital Epidemiology* (formerly *Infection Control*)
	1995-2000	**Founding Editor**, *Clinical Performance and Quality Health Care*
	2001-Current	**Editor-at-Large** *The New England Journal of Medicine* The Editor-at-Large is a position approved by Jeff Drazen, MD, Editor-in-Chief. The responsibilities of the Editor-at-Large include selecting the reviewers, reading the manuscripts, and making final decisions for all manuscripts submitted to the *NEJM* by members of the Editorial Board, Associate or Deputy Editors, or the Editor-in-Chief.
JOURNAL EDITORIAL BOARDS	1979-83	*Antimicrobial Agents and Chemotherapy*
	1979-90	*American Journal of Infection Control*
	1984-90	*Journal of Hospital Infection* (London)
	1990-	*Enfermedades Infecciosas y Microbiologia Clinica* (Journal of the Spanish Society of Infectious Diseases and Clinical Microbiology)
	1992-2000	*The New England Journal of Medicine*
	1993-95	*European Journal of Clinical Microbiology and Infectious Diseases*
	1993-2000	National Foundation for Infectious Diseases Publication "Clinical Updates in Infectious Diseases"
	1993-95	*Journal of Infectious Diseases and Antimicrobial* Agents (Infectious Disease Associates of Thailand)
	1993-1996	*Microbial Drug Resistance*
	1995-2004	*Clinical Infectious Diseases*
	1997-2002	*Sepsis*

	1998-2005	*The American Journal of Medicine*
ADVISORY BOARD	2002-4	Academic Advisory Board of the Pfizer Visiting Professorship Program
MAJOR RESEARCH INTERESTS	1)	Prevention and Control of Hospital-Acquired Infections
	2)	Sepsis
	3)	*Candida* bloodstream infections
	4)	Policy Development for Quality of Care of Patients

FELLOWS TRAINED AND THEIR CURRENT ACTIVITIES

Postdoctoral Fellows Directly Supervised

1974-76 **Robert B. Craven, MD**, Hospital Epidemiologist, Vector Borne Disease Control, Fort Collins, Colorado

1976-77 **James Veazey, MD**, Associate Professor of Medicine, Hospital Epidemiologist, Albany Medical Center, Albany, New York

1976-78 **Timothy Townsend, MD**, Senior Director, Medicial Affairs, Johns Hopkins Hospital, Baltimore, Maryland

1978-79 **Leigh G. Donowitz, MD**, Professor, Pediatrics, University of Virginia, Charlottesville, Virginia

1979-80 **Bruce Hamory, MD**, Associate Professor of Medicine, Hospital Epidemiologist, Hershey Medical Center, Hershey, Pennsylvania

1980-81 **Bruce Farber, MD**, Infectious Diseases Unit, Hospital Epidemiologist, Assistant Professor of Medicine, Cornell Medical School, North Shore University Hospital, Manhasset, New York

1979-81 **William Martone, MD, MS**, Director, Hospital Infection Branch, Centers for Disease Control and Prevention, Atlanta, Georgia

1979-82 **James E. Peacock, MD**, 1982: Associate Professor of Medicine, Bowman-Gray, Winston-Salem, North Carolina

1980-82 **John N. Kreiger, MD**, 1982: Associate Professor Urology, University of Washington, Seattle, Washington

1980-83 **Robert L. Thompson, MS, MD**, 1983: Chief, Department of Internal Medicine, University of Washington, Seattle, Washington

1983-84 **Robert L. Brawley, MS, MD**, 1984: Epidemiologist, U.S. Naval Hosp. San Francisco, California

1983-85 **Charles E. Haley, MS, MD**, 1984: Medical Epidemiologist, San Antonio Health Dept. San Antonio, Texas

1983-85 **Hseih-Shong Leu, MS, MD**, 1985: Hospital Epidemiologist, Chang-Gung Memorial Hospital, Taipei, TAIWAN

1983-85 **Samuel Ponce de Leon, MS, MD**, 1985: Chief, Hospital Epidemiology, Division Instituto de Nutricion, Mexico City, MEXICO

1984-85 **Magued Ishak, MD, MS**, Microbiologist, Hospital Maisonneuve,

Rosemont, Montreal, Quebec, CANADA

1984-85 **Carol Van Dyke Freer, MS, MD**, 1985: Hospital Epidemiologist, Hanover General Hospital, Hanover, Pennsylvania

1984-85 **Allan J. Morrison, MS, MD**, 1985: Hospital Epidemiologist, Fairfax Hospital, Fairfax, Virginia

1986-87 **Sergio Wey, MD**, 1987: Chief of Infectious Diseases Division, Hospital Epidemiologist, Escola Paulista de Medicine, Sao Paulo, BRAZIL

1986-88 **Michael A. Martin, MD**, 1988: Hospital Epidemiologist, Oregon Health Sciences University, Portland, Oregon

1987-89 **Gail Stanley, MD**, 1989: Clinical Assistant Professor of Medicine, Hospital Epidemiologist, University of E. Tennessee, Bristol, TN

1988-89 **Claudio Pannuti, MD**, 1989: Associate Professor of Medicine, Hospital Epidemiologist, Universidade de Sao Paulo, Sao Paulo, BRAZIL

1988-89 **Lisa Veach, MD**, 1989: Infectious Disease Practitioner, Des Moines, Iowa

1988-90 **David Reagan, MD, PhD**, 1990: Assistant Professor of Medicine, East Tennessee State University, Bristol, Tennessee and Chief, Infectious Diseases, VA Medical Center, Bristol, TN

1988-91 **Bradley Doebbeling, MD**, Assistant Professor, Department of Internal Medicine, University of Iowa, Iowa City, Iowa

1988-91 **Trish Perl, MD**, Assistant Professor, Hospital Epidemiologist, Johns Hopkins University, Baltimore, Maryland

1989-91 **Ann Broderick, MD**, Staff Physician, The Free Medical Clinic, Iowa City, Iowa

1989-90 **Heinrich Geiss, MD**, Associate Professor, University of Heidelberg, Heidelberg, GERMANY

1990 **Antoni Trilla, MD, PhD**, Faculty Staff Physician, Infectious Diseases Unit, Hospital Clinic, University of Barcelona, Barcelona, SPAIN

1990-92 **Didier Pittet, MD, MS**, Medecin-Responsable, University Hospital of Geneva, Geneva, SWITZERLAND

1990-92 **Andreas Widmer, MD, MS**, Clinical Epidemiology, University Hospital of Basel, Basel, SWITZERLAND

1991-92 **Javier Ena, MD, PhD**, Department of Internal Medicine, Hospital Gregorio, Maraon, University of Madrid, Madrid, SPAIN

1991-95 **M. Sigfrido Rangel-Frausto, MD,** Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: Instituto Nacional de la Nutricion, Mexico City, MEXICO

1990-92 **Mark Grosserode, MD**, Inter I.D. Inc. Tulsa, Oklahoma

1990-93 **Daniel Nafziger, MD, MS**, Hospital Epidemiologist, Henry Ford Medical Center, Detroit, Michigan

1992-93 **Roman Pallares, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: University of Barcelona, Barcelona, SPAIN

1992-93 **Andreas Voss, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: Munich University Hospital, Munich, GERMANY

1992-93 **Michael Edmond, MD**, MPH, Assistant Professor, Medical College of Virginia, Virginia Commonwealth University. Richmond, Virginia
Home: University of Pittsburgh, Pittsburgh, Pennsylvania

1992-95 **Ed Morales, MD**, Infectious Diseases and Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1993-95 **Todd Wiblin, MD**, Infectious Diseases and Clinical Epidemiology Training. Home: University of Iowa Hospitals and Clinics, Iowa City, Iowa

1993-95 **Marie-Claude Roy, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: Hospital de l'Enfant-Jesus, Quebec, CANADA

1994-95 **Yasmina Berrouane, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: FRANCE

1993-95 **Daniel Diekema, MD**, Infectious Diseases and Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1994-95 **Carl Lebuhn, MD**, Infectious Diseases and Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1994-95 **Patricia Meier, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa
Home: United States Air Force, Texas

1994-95 **Constanze Wendt, MD**, Clinical Epidemiology Training, University of Iowa Hospitals and Clinics, Iowa City, Iowa. Home: GERMANY

1995 **Stefan Weber, MD**, Infectious Diseases and Clinical Epidemiology Training at The University of Iowa. Home: GERMANY

1995-98 **Alice Wong, MD,** Assistant Professor; University of Calgary; Calgary, CANADA

1996-98 **Diane Franchi, MD,** Assistant Professor, Eastern Virginia Medical School Norfolk, Virginia

1997-99 **Werner Bischoff, MD,** Bowman-Grey School of Medicine, North Carolina

2000-02 **Andrea Gonzalez, MD,** Fellow, Infectious Diseases. Medical College of Virginia, VCU, Richmond.

2001-02 **Heike von Baum, MD**. Faculty. University of Heidelberg, Germany.

Other Postdoctoral Fellows Trained

1989-90 **Karen Maves, MD**, Associate, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1989-91 **Ricardo Ciniglio, MD**, Cardiology Fellow, Department of Internal Medicine, University of Nebraska, Omaha, Nebraska

1989-91 **Brenda Phillips, MD**, University of Iowa Faculty, General Medicine Fellowship, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1989-91 **Tina Wald, MD**, Fellow, Infectious Diseases and Geriatrics, Department of Internal Medicine, University of Wisconsin Hospital and William S. Middleton Memorial Veterans Hospital, Madison, Wisconsin

1991-92 **Gregory Bottei, MD**, Pulmonary Fellow, Division of Pulmonary Diseases, University of North Carolina-Chapel Hill

1991-92 **Ghaly Kerolus, MD**, Morgan County Medical Associates, Berkely Spring, West Virginia

1991-93 **Issa Ephtimios, MB, CHB**, Division of Infectious Diseases, Henderson General Hospital, McMaster Medical Unit, Hamilton, Ontario, CANADA

1992-94 **Leon Menajovsky, MD**, Staff physician, Department of Medicine, Des Moines Veterans Affairs Medical Center. Currently Assistant Professor, Division of General Medicine, Jefferson Medical College, Philadelphia, Pennsylvania.

1992-93 **Rebecca Hegeman, MD**, Fellow Associate, Department of Internal Medicine-Nephrology, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1993-95 **Iftekhar Awan, MD**, General Medicine Fellowship, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa

1994-95 **Nicole Levstik, MD**, General Medicine Fellowship, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, Iowa

PhD Theses Directed

1988 **Louise Ann McNutt, MS, PhD**, "Risk Factors for Nosocomial Pneumonia in Medical Intensive Care Unit Patients." Current Position: Center for Disease Control, EIS Officer, Atlanta, Georgia

1990 **Shin H. Chung**, "Risk Factors for Hospital-Acquired Pulmonary Emboli"

1992 **Ning Li**, "Categorical Data Analysis of Risk Factors for Nosocomial Infections"

1993-95 **Deborah Schroeder**, "Hospital-Acquired Urinary Tract Infections"

BIBLIOGRAPHY

Text Books

1. *Handbook on Hospital Acquired Infections*. RP Wenzel, ed. Boca Raton, Fla: CRC Press, Inc.; 1981.

2. *Prevention and Control of Nosocomial Infections*. RP Wenzel, ed. Baltimore, Md: Williams and Wilkins; 1987.

3. *Assessing Quality Health Care: Perspective for Clinicians*. RP Wenzel, ed. Baltimore, Md: Williams and Wilkins; 1992.

4. *Prevention and Control of Nosocomial Infections.* 2nd edition. RP Wenzel, ed. Baltimore, Md: Williams and Wilkins; 1993.

5. *Prevention and Control of Nosocomial Infections.* 3rd edition. RP Wenzel, ed. Baltimore, Md: Williams and Wilkins, 1997.

6. *Prevention and Control of Nosocomial Infections.* 4th edition. RP Wenzel, ed. Baltimore. Lippincott, Williams and Wilkins; 2003.

7. Clinical Decision Support: Hospital Infection Control. Richard P Wenzel, and Gonzalo Bearman eds. Decision Support in Medicine 2014. LLC, Wilmington, DE

8. Clinical Decision Support: Infectious Diseases. RP Wenzel, Associate Editor, Decision Support in Medicine 2014. LLC Wilmington, DE.

Journal/Book Section Editor

1. Nosocomial Infections. *Current Opinion in Infectious Diseases*. Current Science, London, 1988.

2. Nosocomial and Community Infections: the Role of the Clinical Microbiology Laboratory. *Manual of Clinical Microbiology*. 5th ed. A Balows, ed. Washington, D.C.: American Society for Microbiology; 1990.

3. The Control of Communicable Diseases. *Public Health and Preventive Medicine*. 13th Edition. JM Last, R Wallace, eds. Norwalk, Conn: Appleton & Lange; 1991.

4. Nosocomial Infections. *Current Opinion in Infectious Diseases*. London: Current Science; 1990.

5. Nosocomial Infections. *Manual of Clinical Microbiology*. 6th ed. Washington D.C.: American Society for Microbiology; 1994.

6 . Staphylococcal Infections. *J Chemotherapy*. 1994; 6:(suppl 2)1-75.

7. Nosocomial Infections. *Manual of Clinical Microbiology.* 7th ed. Washington, DC.:American Society for Microbiology; 1999

Books for General Readership

1. *Stalking Microbes. A Relentless Pursuit of Infection Control.* (non-fiction) Richard P. Wenzel. 2005 Author House. Bloomington, Indiana. ISBN: I-4208-2006-0(so); ISBN:I-4208-2005-2(dj). Library of Congress Control Number 2004195076

2. *Labyrinth of Terror* Fiction – Medical Thriller) Richard P. Wenzel, 2010. Brandylane Publishers, Inc. Richmond, Virginia ISBN 978-1-88391393
Library of Congress Number 2010934024
. Nominated – Best Fiction Award – Virginia Library Association

Monographs

1. Jones RN, Koontz, FP, Stratton CW IV, Wenzel RP. *Emerging Trends in Gram-Negative Resistance. A New Concern for Critical Care Medicine.* Lederle Laboratories Publication; 1990.

2. Doebbeling BN, Herwaldt L, Nettleman M, Pfaller MA, Wenzel RP. *Hospital-Acquired Infections: New Challenges.* The Upjohn Company; 1991.

3. *A Guide to Infection Control in the Hospital*. Editors: Wenzel RP, Edmond M, Pittet D, Devaster J-M, Geddes A, Butzler J-P. Hamilton, London: B.C. Decker Inc., 1998. Croatian translation - 1999; Spanish translation - 2000; Polish translation - 2001. 2nd edition - 2002. French translation - 2002. Greek translation - 2002. Russian translation - 2003. 3rd edition - 2004. 4th edition – 2008 with Chinese translation in 2008.
Over 60,000 copies have been distributed free of charge to health care workers in the developing world coutriesby the end of 2008

Papers

1. Perkins JC, Tucker DN, Knopf HLS, Wenzel RP, Hornick RB, Kapikian AZ, Chanock RM. Evidence for protective effect of an inactivated rhinovirus vaccine administered by the nasal route. *Am J Epidemiol*. 1969; 90:319-326.

2. Perkins JC, Tucker DN, Knopf HLS, Wenzel RP, Kapikian AZ, Chanock RM. Comparison of protective effect of neutralizing antibody in serum and nasal secretions in experimental rhinovirus type 13 illness. *Am J Epidemiol.* 1969;90:519-526.

3. Biggs RD Jr, Wenzel RP. Cardiac irritability secondary to sympathetic overactivity. *Md State Med J.* 1970; 19:97-98.

4. Music SI, Libonati JP, Wenzel RP, Snyder MJ, Hornick RB , Woodward TE. Induced human cholera. *Antimicrob Agents Chemother.* 1970; 10:462-466.

5. Wenzel RP, McCormick DP, Smith EP, Clark DL, Beam WE Jr. Acute respiratory disease: clinical and epidemiologic observations of military trainees. *Milit Med.* 1971; 136:873-880.

6. Wenzel RP, Phillips RA. Intraperitoneal infusions for initial therapy of cholera. *Lancet*. 1971; 2:494-495.

7. Wenzel RP, McCormick DP, Le Bouvier GL. Arthritis and hepatitis. *N Engl J Med*. 1971; 285:805.

8. Hornick RB, Music SI, Wenzel RP, Cash R, Libonati JP, Snyder MJ, Woodward TE. The Broad Street Pump revisited: response of volunteers to ingested cholera vibrios. *Bull NY Acad Med*. 1971; 47:1181-1191.

9. Wenzel RP, Mitzel JR, Davies JA, Beam WE Jr. Meningococcal infection: clinical and epidemiologic observations on a military base over a one-year period. *U.S. Naval Medical Field Research Laboratory, Camp Lejuene, North Carolina*. Vol XXI:1-7, 1971. Bureau of Medicine and Surgery, Navy Department Work Unit MF 12.524.009-8011BF61.4.

10. Wenzel RP, Le Bouvier GL , Beam WE Jr. Drug abuse and viral hepatitis in marines. *JAMA*. 1972; 220:707-709.

11. Wenzel RP, Mitzel JR, Davies JA, Beam WE Jr. Serum and nasal secretion immune response in meningococcal disease. *Infect Immun*. 1972; 5:627-629.

12. Wenzel RP, McCormick DP, Beam WE Jr. Parainfluenza pneumonia in adults. *JAMA*. 1972; 221:294-295.

13. Wenzel RP. Venn diagrams in drug abuse education. *JAMA*. 1972; 220:860-861.

14. McCormick DP, Wenzel RP, Smith EP, Beam WE Jr. Failure of rifampin to inhibit adenovirus replication. *Antimicrob Agents Chemother*. 1972; 2:326-328.

15. McCormick DP, Wenzel RP, Davies JA, Beam WE Jr. Nasal secretion protein responses in patients with wild-type adenovirus disease. *Infect Immun*. 1972;6:282-288.

16. Wenzel RP, McCormick DP, Busch HJ, Beam WE Jr. Arthritis and viral hepatitis. A patient with transient serum hepatitis-associated antigen, skin nodules, rash, and low serum complement. *Arch Intern Med*. 1972; 130:770-771.

17. Wenzel RP, Stotka VL. Imported malaria in Marine Corps personnel. *N Engl J Med*. 1972; 287:1153.

18. McCormick DP, Wenzel RP, Beam WE Jr. Lifelong recurrent cutaneous Herpesvirus hominus infection. *U.S. Naval Medical Field Research Laboratory, Camp Lejeune, North Carolina*. Vol XXII, No. 21, August 1972. Bureau of Medicine and Surgery, Navy Department Work Unit MF51.1524.009-8011BF61.9.

19. Wenzel RP, Adams JF, Smith EP. Patterns of illicit drug use in viral hepatitis patients. *Milit Med*. 1973; 138:345-350.

20. Wenzel RP, McCormick DP, Beam WE Jr. Clinical applications of Australia/Hepatitis-associated antigen. *South Med J*. 1973; 66:186-189.

21. Stotka VL, Wenzel RP. Malaria in Vietnam (I Corps Sector): review of 214 cases including EEG patterns on 19 acutely ill patients. *Milit Med*. 1973; 138:795-802.

22. Wenzel RP, Mitzel JR, Davies JA, Edwards EA, Berling C, McCormick DP, Beam WE Jr. Antigenicity of a polysaccharide vaccine from *Neisseria meningitidis*,administered intranasally. *J Infect Dis*. 1973; 128:31-40.

23. Hendley JO, Wenzel RP, Gwaltney JM Jr. Transmission of rhinovirus colds by self-inoculation. *N Engl J Med*. 1973; 288:1361-1364.

24. Wenzel RP, McCormick DP, Davies JA, Berling C, Beam WE Jr. Cytomegalovirus infection: a seroepidemiologic study of a recruit population. *Am J Epidemiol*. 1973; 97:410-414.

25. Wenzel RP, Hendley JO, Sande MA, Gwaltney JM Jr. Revised (1972-1973) bivalent influenza vaccine. Serum and nasal antibody responses to parenteral vaccination. *JAMA*. 1973; 226:435-438.

26. Wenzel RP, Davies JA, Mitzel JR, Beam WE Jr. Non-usefulness of meningococcal carriage-rates. *Lancet*. 1973; 2:205.

27. Wenzel RP. Food Poisoning. *Current Therapy 1974*. HF Conn, ed. Philadelphia, Pa: W.B. Saunders Co.; 1974:23-26.

28. Cash RA, Music SI, Libonati JP, Snyder MJ, Wenzel RP, Hornick RB. Response of man to infection with *Vibrio cholerae*. I. Clinical, Serologic, and bacteriologic responses to a known inoculum. *J Infect Dis*. 1974; 129:45-52.

29. McCormick DP, Wenzel RP, Senterfit LB, Beam WE Jr. Relationship of pre-existing antibody to subsequent infection by *Mycoplasma pneumoniae* in adults. *Infect Immun*. 1974; 9:53-59.

30. *University of Virginia Medical Center Isolation Procedure and Infection Control Manual*. Revised 1973. Prepared by RP Wenzel, CA Osterman and GL Mandell. Reynolds Printing Company, Charlottesville, Virginia 1973.

31. Sande MA, Wenzel RP. Meningococcal meningitis and meningococcemia. *Va Med Mo*. 1974; 101:386-393.

32. Wenzel RP, Hendley JO, Davies JA, Gwaltney JM Jr. Coronavirus infections in military recruits: three-year study with coronavirus strains OC43 and 229E. *Am Rev Respir Dis*. 1974; 109:621-624.

33. Hamory BH, Osterman CA, Wenzel RP. Herpetic whitlow. Letter to the Editor. *N Engl J Med*. 1975; 292:268.

34. Wenzel RP, Teates CD, Galapon Q, Barczak R, Ling C, Overby LR. Acute viral hepatitis in adults. Comparison of the radioimmunoassay and counter-immunoelectrophoresis methods of detecting HBAg. *JAMA*. 1975; 232:366-368.

35. Craven RB, Wenzel RP, Atuk NO. Minimizing tuberculosis risk to hospital personnel and students exposed to unsuspected disease. *Ann Intern Med*. 1975; 82:628-632.

36. Wenzel RP, Hendley JO, Craven RB, Gwaltney JM Jr. Antibody Responses to A/30-C/707 and A/X-37 Influenza Vaccines. *Proceedings of the 1st Intersectional Conference of the International Association of Microbiological Societies.* Tokyo, 1-7 September, 1974;4:184-197, 1975.

37. Sande MA, Gadot F, Wenzel RP. Point source epidemic of *Mycoplasma pneumoniae* infection in a prosthodontics laboratory. *Am Rev Respir Dis.* 1975;112:213-217.

38. Wenzel RP, Osterman CA, Hunting KJ, Gwaltney JM Jr. Hospital-acquired infections. I. Surveillance in a university hospital. *Am J Epidemiol*. 1976;103:251-260.

39. Wenzel RP, Hunting KJ, Osterman CA, Sande MA. *Providencia stuartii*, a hospital pathogen: Potential factors for its emergence and transmission. *Am J Epidemiol*. 1976; 104:170-180.

40. Mason RA, Wenzel RP, Seligmann EB, Ginn RK. A reference, inactivated, epidemic typhus vaccine: Laboratory evaluation of candidate vaccines. *J Biol Stand*. 1976; 4:209-216.

41. Thompson RL, Sande MA, Wenzel RP, Hoke CH, Gwaltney JM Jr. Swine-influenza infection in civilians. *N Engl J Med*. 1976: 295:714-715.

42. Wenzel RP, Osterman CA, Hunting KJ. Hospital-acquired infections II. Infection rates by site, service and common procedures in a university hospital. *Am J Epidemiol*. 1976; 104:645-651.

43. Guerrant RL, Dickens MD, Wenzel RP, Kapikian AZ. Toxigenic bacterial diarrhea: nursery outbreak involving multiple bacterial strains. *J Pediatr*. 1976; 89:885-891.

44. Wenzel RP, Hendley JO, Dodd WK, Gwaltney JM Jr. Comparison of josamycin and erythromycin in the therapy of *Mycoplasma pneumoniae*, pneumonia. *Antimicrob Agents Chemother*. 1976; 10:899-901.

45. Wenzel RP, Craven RB, Davies JA, Hendley JO, Hamory BH, Gwaltney JM Jr. Field trial of an inactivated *Mycoplasma pneumoniae* vaccine. I. Vaccine efficacy. *J Infect Dis*. 1976; 134:571-576.

46. Craven RB, Wenzel RP, Calhoun AM, Hendley JO, Hamory BH, Gwaltney JM Jr. Comparison of the sensitivity of two methods for isolation of *Mycoplasma pneumoniae. J Clin Microbiol*. 1976; 4:225-226.

47. Suratt PM, Gruber B, Wellons HA, Wenzel RP. Absence of clinical pneumonia following bronchoscopy with contaminated and clean bronchofiberscopes. *Chest*. 1977; 71:52-54.

48. McCarthy MF Jr, Wenzel RP. Postoperative spinal fluid infections after neurosurgical shunting procedures. *Pediatrics*. 1977; 59:793.

49. Wenzel RP, Craven RB, Davies JA, Hendley JO, Hamory BH, Gwaltney JM Jr. Protective efficacy of an inactivated *Mycoplasma pneumoniae* vaccine. *J Infect Dis*. 1977; 136:S204-S207.

50. Wenzel RP, Hunting KJ, Osterman CA. Postoperative wound infection rates. *Surg Gynecol Obstet.* 1977; 144:749-752.

51. Wenzel RP. The Infectious Mononucleosis Syndrome. *Current Concepts of Infectious Diseases.* EW Hook, GL Mandell, JM Gwaltney, MA Sande, eds. New York, NY: John Wiley & Sons; 1977:167-178.

52. Green JW, Wenzel RP. Postoperative wound infections: a controlled study of the increased duration of hospital stay and direct cost of hospitalization. *Ann Surg*. 1977; 185:264-268.

53. Guerrant RL, Strausbaugh LJ, Wenzel RP, Hamory BH, Sande MA. Nosocomial bloodstream infections caused by gentamicin-resistant gram negative bacilli. *Am J Med.* 1977; 62:58-64.

54. Wenzel RP, Deal EC, Hendley JO. Hospital-acquired viral respiratory illness on a pediatric ward. *Pediatrics*. 1977; 60:367-371.

55. Rose R, Hunting KJ, Townsend TR, Wenzel RP. Morbidity/Mortality and economics of hospital-acquired blood stream infections: a controlled study. *South Med J*. 1977; 70:1267-1269.

56. Wenzel RP, Veazey JM Jr, Townsend TR. Role of the inanimate environment in hospital-acquired infections. *Infection Control in Health Care Facilities - Microbiological Surveillance*. Baltimore, MD: University Park Press; 1977:71-143.

57. Hamory BH, Wenzel RP. Hospital-associated candiduria: predisposing factors and review of the literature. *J Urol.* 1978; 120:444-448.

58. Wenzel RP. Infection surveillance systems. Choosing an approach for your hospital. *Proceedings of Association for Practitioners in Infection Control*. 1977, 1978.

59. Wenzel RP. Hospital surveillance of community infections. *Proceedings of Association for Practitioners in Infection Control.* 1977, 1978.

60. Wenzel RP. Hospital-acquired infections: a medical and economic problem. *Va Med.* 1978; 105:429-430.

61. Wenzel RP. The high rate of infection in the newborn intensive care unit (Editorial). *Drug Ther*. 1978; 3:17-18.

62. National Coordinating Committee on Large Volume Parenterals (includes R.P. Wenzel.) Recommended procedures for in-use testing of large volume parenterals suspected of contamination or of producing a reaction in a patient. *Am J Hosp Pharm*. 1978; 35:678-682.

63. Wenzel RP. Nosocomial infections; surveillance. *Principles and Practice of Infectious Diseases.* GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley & Sons, Inc.; 1979:2213-2219.

64. Wenzel RP. Nosocomial infections; sterilization, disinfection, and disposal of hospital waste. *Principles and Practice of Infectious Diseases*. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley & Sons, Inc.; 1979:2219-2224.

65. Wenzel RP. Nosocomial infections; organization for infection control. *Principles and Practice of Infectious Diseases.* GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley & Sons, Inc.; 1979:2224-2227.

66. Veazey JM, Wenzel RP. Nosocomial infections; nosocomial pneumonia. *Principles and Practice of Infectious Diseases*. GL Mandell, RG Douglas, JE Bennett eds. New York, NY: John Wiley & Sons, Inc.; 1979:2228-2234.

67. Wenzel RP. Nosocomial infections; nosocomial urinary tract infection. *Principles and Practice of Infectious Diseases*. GL Mandell, RG Douglas, JE Bennett eds. New York, NY: John Wiley & Sons, Inc.; 1979:2234-2237.

68. Wenzel RP. Nosocomial infections; nosocomial viral hepatitis. *Principles and Practice of Infectious Diseases*. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley & Sons, Inc.; 1979:2238-2241.

69. Townsend TR, Wenzel RP. Nosocomial infections; nosocomial viral respiratory infections in pediatrics, nosocomial blood stream infections, isolation, and protective environments. *Principles and Practice of Infectious Diseases.* GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley & Sons, Inc.; 1979:2242-2247.

70. Tully JG, Rose DL, Whitcomb RF, Wenzel RP. Enhanced isolation of *Mycoplasma pneumoniae* from throat washings with a newly modified culture medium. *J Infect Dis*. 1979; 139:478-482.

71. Donowitz LG, Marsik FJ, Hoyt JW and Wenzel RP. *Serratia marcescens* bacteremia from contaminated pressure transducers. *JAMA*. 1979; 242:1749-1751.

72. Wenzel RP, Sande MA, Townsend TR, Levine, JI. A statewide program to study the relationship of aminoglycoside usage in hospitals and patterns of antibiotic resistance in clinically important gram-negative rod isolates. *Practical Aspects of Antibiotic Review*. CM Kunin, ed. Atlanta, Ga: American Health Consultants; 1979:265-271.

73. Wenzel RP. Antibiotic audit approaches for the small hospital. *Practical Aspects of Antibiotic Review*. CM Kunin, ed. Atlanta, Ga: American Health Consultants; 1979:227-238.

74. Wenzel RP, Osterman CA, Townsend TR, Veazey JM Jr, Servis KH, Miller LS, Craven RB, Miller GB Jr, Jackson RS. Development of a statewide program for surveillance and reporting of hospital-acquired infections. *J Infect Dis*. 1979; 140:741-746.

75. Givens CD, Wenzel RP. Catheter-associated urinary tract infections in surgical patients: a controlled study on the excess morbidity and costs. *J Urol*. 1980; 124:646-648.

76. Donowitz LG, Wenzel RP. Endometritis following cesarean section. A controlled study of the increased duration of hospital stay and direct cost of hospitalization. *Am J Obstet Gynecol*. 1980; 137:467-469.

77. Gardner P, Bennett JV, McGowan JP, Wenzel RP. Control of aminoglycoside resistant organisms in the hospital (Editorial). *J Infect Dis*. 1980; 141:415.

78. Wenzel RP, Schaffner W. Of Roman gods and a new journal (Editorial). *Infect Control*. 1980; 1:13.

79. Townsend TR, Rudolf LE, Westervelt FB Jr, Mandell GL, Wenzel RP. Prophylactic antibiotic therapy with cefamandole and tobramycin for patients undergoing renal transplantation. *Infect Control*. 1980; 1:93-96.

80. Farber BF, Wenzel RP. Postoperative wound infection rates: results of prospective statewide surveillance. *Am J Surg*. 1980; 140:343-346.

81. Peacock JE, Marsik FJ, Wenzel RP. Methicillin-resistant *Staphylococcus aureus*: introduction and spread within a hospital. *Ann Intern Med*. 1980; 93:526-532.

82. Wenzel RP. Focus on nosocomial infections: the Israeli method (Editorial). *Infect Control*. 1980; 1:226.

83. Wenzel RP, Osterman CA, Miller GB Jr, Gröschel DHM. Ein zentrales freiwilliges Programm zur Uberwachung and Registrierung von Hospitalinfektionen im Bundesstaat Virginia. *Hygiene und Medizin*. 1980; 5:603-605.

84. Wenzel RP. Surveillance and reporting of hospital acquired infections. *Handbook of Hospital Acquired Infections.* RP Wenzel, ed. Boca Raton, Fla: CRC Press, Inc.; 1981:35-72.

85. Wenzel RP, Osterman CA, Mandell GL. University of Virginia Medical Center isolation procedure and infection control manual. *Handbook on Hospital Acquired Infections*. RP Wenzel, ed. Boca Raton, Fla: CRC Press, Inc.;1981:127-209.

86. Atuk NO, Townsend TR, Hunt EH, Wenzel RP. An employee health service for infection control. *Handbook on Hospital Acquired Infections*. RP Wenzel, ed. Boca Raton, Fla: CRC Press, Inc.; 1981:211-250.

87. Wenzel RP. Working Through an Antibiotic Review of 1-100 Bed Community Hospitals. *Proceedings of the First National Conference on Antibiotic Review, West Coast Update.* Los Angeles, 1981.

88. Wenzel RP, Farber BF. Standards for minimizing hospital-acquired (nosocomial) infections. *Lawyers' Medical Cyclopedia 1981*. CJ Frankel, ed. Indianapolis, Ind: Allen Smith Publications; 1981: 565-572, revised 1981.

89. Townsend TR, Wenzel RP. Nosocomial bloodstream infections in a newborn intensive care unit. *Am J Epidemiol*. 1981; 114:73-80.

90. Wenzel RP, Osterman CA, Donowitz LG, Hoyt JW, Sande MA, Martone WJ, Peacock JE Jr, Levine JI, Miller GB Jr. Identification of procedure-related nosocomial infections in high-risk patients. *Rev Infect Dis*. 1981; 3:701-707.

91. Donowitz LG, Marsik FJ, Fisher KA, Wenzel RP. Contaminated breast milk: a source of Klebsiella,bacteremia in a newborn intensive care unit. *Rev Infect Dis*. 1981; 3:716-720.

92. Martone WJ, Osterman CA, Fisher KA, Wenzel RP. *Pseudomonas cepacia*: implications and control of epidemic nosocomial colonization. *Rev Infect Dis*. 1981; 3:708-715.

93. Farber BF, Kaiser DL, Wenzel RP. Relation between surgical volume and incidence of postoperative wound infection. *N Engl J Med*. 1981; 305:200-204.

94. Wenzel RP, Landry SL, Russell BS, Donowitz LG, Thompson RL, Hoyt JW, Thompson SY, Miller GB, Jr. Prevention and control of nosocomial infections in intensive care patients. *Proceedings of Internationales Symposium uber aktuelle Probleme der Notfallmedizin und Intensivtherapie in Munster*. Infektion – Sepsis - Peritonitis. Georg Thieme Verlag Stuttgart, 1981.

95. Peacock JE, Moorman DR, Wenzel RP, Mandell GL. Methicillin-resistant *Staphylococcus aureus*: microbiologic characteristics, antimicrobial susceptibilities, and assessment of virulence of an epidemic strain. *J Infect Dis*. 1981; 144:575-582.

96. Wenzel RP. Diagnostico e tratamento das infeccoes *por Mycoplasma pneumoniae. Ciencia Cultura Saude.* 1981; 3:46-49.

97. Wenzel RP. Isolation and the environment in preventing hospital infections. *Proceedings of the International Symposium on Hospital Acquired Infections.* Mexico City, November 1981.

98. Wenzel RP, Thompson RL. Hospital acquired bloodstream infections. *Proceedings of the International Symposium on Hospital Acquired Infections.* Mexico City, November 1981.

99. Wenzel RP, Landry SL, Haley CE, Thompson RL. Outbreaks of hospital acquired infections. *Proceedings of the International Symposium on Hospital Acquired Infections*. Mexico City, November 1981.

100. Wenzel RP, Landry SL, Cabezudo I. Special problems in infection control: the intensive care areas, the renal transplant service, the employee health services, and monitoring autoclaves in the hospital. *Proceedings of the International Symposium on Hospital Acquired Infections*. Mexico City, November 1981.

101. Shands JW, Wenzel RP, Wolff SM, Eickhoff TC, Fields BN, Jackson GG. Hospital epidemiology and infection control: the changing role of the specialist in infectious diseases. *J Infect Dis*. 1981; 144:609-613.

102. Wenzel RP, Donowitz LG, Miller GB. Methicillin-resistant *Staphylococcus aureus* United States. *MMWR*. April 1981; 140-147.

103. Mayo JW, Wenzel RP. Rates of hospital-acquired bloodstream infections in patients with specific malignancy. *Cancer*. 1982; 50:187-190.

104. Senterfit LB, Tully JG, Rose DL, Wenzel RP. A reevaluation of serologic and culture data from an inactivated *Mycoplasma pneumonia* vaccine field trial. *Bacterial Vaccines Volume IV: Seminars in Infectious Disease*. L Weinstein, B Fields, eds. New York, NY: Thieme-Stratton Inc.; 1982:198-200.

105. Wenzel RP. Prevention and treatment of hospital acquired infections. *Cecil Textbook of Medicine*. JB Wyngaarden, LH Smith, eds. Philadelphia, Pa: W.B. Saunders, Co.; 1982:1402-1409.

106. Thompson RL, Fisher KA, Wenzel RP. In vitro activity of N-formimidoyl thienamycin and other beta-lactam antibiotics against methicillin-resistant *Staphylococcus aureus. Ann Intern Med*. 1982; 21:341-343.

107. Thompson RL, Cabezudo I, Wenzel RP. Epidemiology of nosocomial infections caused by methicillin-resistant *Staphylococcus aureus. Ann Intern Med*. 1982; 97:309-317.

108. Landry SL, Donowitz LG, Wenzel RP. Hospital-wide surveillance: perspective for the practitioner. *Am J Infect Control*. 1982; 10:66-67.

109. Donowitz LG, Wenzel RP, Hoyt JW. The high risk of hospital-acquired infection in the ICU patient. *Crit Care Med*. 1982; 10:355-357.

110. Wenzel RP. The emergence of methicillin-resistant *Staphylococcus aureus* (editorial). *Ann Intern Med.* 1982; 97:440-442.

111. Thompson RL, Wenzel RP. International recognition of methicillin-resistant strains of *Staphylococcus aureus* (editorial). *Ann Intern Med.* 1982; 97:925-926.

112. Hoyt JW, Donowitz LG, Wenzel RP. Nosocomial infections in critically ill patients. *Ear Nose Throat J.* 1982; 61:March.

113. Krieger JN, Kaiser DL, Wenzel RP. Nosocomial urinary tract infections: secular trends, treatment and economics in a university hospital. *J Urol*. 1983; 130:102-106.

114. Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of bloodstream infections in hospitalized patients. *J Infect Dis*. 1983; 148:57-62.

115. Krieger JN, Kaiser DL, Wenzel RP. Nosocomial urinary tract infections cause wound infections postoperatively in surgical patients. *Surg Gynecol Obstet*. 1983; 156:313-318.

116. Cross A, Allen J, Burke J, Ducel G, Harris A, John J, Johnson D, Lew M, MacMillan B, Meers P, Skalova R, Wenzel R, Tenny J. Nosocomial infections due to *Pseudomonas aeruginosa*: review of recent trends. *Rev Infect Dis*. 1983; 5:S837-842

117. Wenzel RP, Townsend TR. When can the infected hospital employee return to work? *Current Clinical Topics in Infectious Diseases*. 4th Edition. JS Remington, NM Swartz, eds. New York, NY: McGraw-Hill, Inc.; 1983:75-97.

118. Farber BF, Wenzel RP. Hospital acquired pneumonia. *Internal Medicine: A Systematic Approach.* JH Stein, MA Sande, eds. Boston, Mass: Little Brown and Company; 1983:1195-1197.

119. Farber BF, Wenzel RP. Hospital infection control. *Internal Medicine: A Systematic Approach.* JH Stein, MA Sande, eds. Boston, Mass: Little Brown and Company; 1983:1152-1156.

120. Fisher G, Wenzel RP. Skin and subcutaneous infections and the syndrome of fever and rash. *Internal Medicine: A Systematic Approach*. JH Stein, MA Sande, eds. Boston, Mass: Little Brown and Company; 1983:1217-1221.

121. Wenzel RP, Thompson RL, Landry SM, Russel BS, Miller PJ, Ponce de Leon S, Miller GB. Hospital-acquired infections in intensive care unit patients: an overview with emphasis on epidemics. *Infect Control.* 1983; 4:371-375.

122. Thompson RL, Haley CE, Searcy MA, Guenthner SM, Kaiser DL, Gröschel DHM, Gillenwater JY, Wenzel RP. Catheter- associated bacteriuria: failure to reduce attack rates using periodic instillations of a disinfectant into urinary drainage systems. *JAMA*. 1984; 251:747-751.

123. Cabezudo I, Thompson RL, Selden RF, Guenthner SH, Wenzel RP. Cefsulodin sodium therapy in cystic fibrosis patients. *Antimicrob Agents Chemother.* 1984; 25:4-6.

124. Young LS, Wenzel RP, Sabath LD, Pollack M, Pennington JE, Platt R. The outlook for prevention and treatment of infections due to *Pseudomonas aeruginosa. Rev Infect Dis*. 1984; 6(S):769-776.

125. Ponce de Leon S, Critchley S, Wenzel RP. Polymicrobial bloodstream infections related to prolonged vascular catheterization. *Crit Care Med.* 1984; 12:856-859.

126. Ponce de Leon S, Wenzel RP. Hospital-acquired bloodstream infections with *Staphylococcus epidermidis*: review of 100 cases. *Am J Med*. 1984; 77:639-644.

127. Morrison AJ, Wenzel RP. Epidemiology of infections due to *Pseudomonas aeruginosa. Rev Infect Dis.* 1984; 6:S627-S642.

128. Wenzel RP, Thompson RL. Nosocomial urinary tract infections. *Principles and Practice of Infectious Diseases.* 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1625-1627.

129. Wenzel RP. Surveillance. *Principles and Practice of Infectious Diseases*. 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1604-1608.

130. Wenzel RP, Gröschel DHM. Sterilization, disinfection, and disposal of hospital waste. *Principles and Practice of Infectious Diseases*. 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1609-1612.

131. Wenzel RP. Organization for infection control. *Principles and Practice of Infectious Diseases.* 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1602-1604.

132. Wenzel RP. Nosocomial viral hepatitis. *Principles and Practice of Infectious Diseases.* 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1627-1630.

133. Wenzel RP, Townsend TR. Isolation. *Principles and Practice of Infectious Diseases*. 2nd Edition. GL Mandell, RG Douglas, JE Bennett , eds. New York, NY: John Wiley and Sons; 1984:1608-1609.

134. Guenthner SH, Wenzel RP. In vitro activities of teichomycin, fusidic acid, flucloxacillin, fosfomycin and vancomycin against methicillin-resistant *Staphylococcus aureus. Antimicrob Agents Chemother*. 1984; 26:268-269.

135. Gröschel DHM, Dwork KG, Wenzel RP, Scheibel LW. First aid after exposure to infectious agents. *Manual Of Laboratory Safety*. BM Miller, ed. Washington, D.C.: American Society for Microbiology, ASM Publications; 1984.

136. Wenzel RP. Hospital acquired infections in the United States special reference to infections in critical care units. *Epidemiological Knowledge and Actions for Hospital Infection Control.* Proceedings of the Verona Congress. 1984.

137. Brawley RL, Wenzel RP. An algorithm for chickenpox exposure. *Pediatr Infect Dis*. 1984; 3:502-504.

138. Brandt SJ, Thompson RL, Wenzel RP. Mycotic pseudoaneurysm of an aortic bypass graft and contiguous vertebral osteomyelitis due to *Aspergillus fumigatus. Am J Med*. 1985; 79:259-262.

139. Wenzel RP. Infection Control Priorities in Critical Care Medicine: Device-Associated Intravascular Infections. *Manual of Clinical Microbiology.* Fourth edition. Washington, D.C.: American Society for Microbiology, ASM Publications; 1985:123-128.

140. Miller PJ, O Connell J, Leipold A, Wenzel RP. Potential liability for transfusion-associated AIDS. *JAMA*. 1985; 253:3419-3424.

141. Salata RA, Gebhart RL, Palmer DL, Wade BH, Scheld WM, Gröschel DHM, Wenzel RP, Mandell GL, Duma RJ. Pneumonia treated with imipenem/cilastatin. *Am J Med* .1985; 78:104-109.

142. Morrison AJ Jr, Wenzel RP. Rabies: a review and current approach for the clinician. *South Med J*. 1985; 78:1211-1218.

143. Norris SM, Guenthner SH, Wenzel RP. Comparative activity of seven extended-spectrum cephalosporins against gram-negative bacilli from blood cultures. *J Antimicrob Chemother*. 1985; 16:183-188.

144. Wenzel RP, Schaffner WM. Infection control a progress report (editorial*). Infect Control.* 1985; 6:9-10.

145. Ishak MA, Gröschel DHM, Mandell GL, Wenzel RP. Association of slime with pathogenicity of coagulase-negative staphylococci causing nosocomial septicemia. *J Clin Microbiol.* 1985; 22:1025-1029.

146. Wenzel RP. Nosocomial infections, diagnosis-related groups, and study on the efficacy of nosocomial infection control. Economic implications for hospitals under the prospective payment system. *Am J Med.*1985; 78:3-7.

147. Donowitz LG, Corrigan C, Crosby IK, Wenzel RP, Hoyt JW. Avoiding infection following pulmonary artery catheterization. *Infect Surg*. 1985; 4:759-762.

148. Wenzel RP, Morrison AJ, Stillman R, Landry S, Ishak M, Haley R, Freer C, Norris S, Searcy MA, Ponce de Leon S. The Re-emergence of Gram-Positive Cocci as Major Nosocomial Pathogens. *Proceedings of the 14th International Congress of Chemotherapy*. Kyoto, Japan, University of Tokyo Press, 1985.

149. Wenzel RP, Hayden FG, Gröschel DHM, Salata RA, Young WS, Greenlee JE, Newman S, Miller PJ, Hechemy KE, Burgdorfer W, Peacock MG, Rubinstein LJ. Acute febrile cerebrovasculitis: a syndrome of unknown, perhaps rickettsial, cause. *Ann Intern Med*. 1986; 104:606-615.

150. Wenzel RP. The evolving art and science of hospital epidemiology. *J Infect Dis*. 1986; 153:462-470.

151. Morrison AJ, Hoffmann KK, Wenzel RP. Associated mortality and clinical characteristics of nosocomial *Pseudomonas maltophilia* in a university hospital. *J Clin Microbiol.* 1986; 24:52-55.

152. Morrison AJ, Gratz J, Cabezudo I, Wenzel RP. The efficacy of several new handwashing agents for removing non-transient bacterial flora from hands. *Infect Control*. 1986; 7:268-272.

153. Ponce de Leon S, Guenthner S, Wenzel RP. Microbiologic studies of coagulase-negative staphylococci isolated from patients with nosocomial bacteremias. *J Hosp Infect*. 1986; 7:121-129.

154. Guenthner SH, Chao HP, Wenzel RP. Synergy between amikacin and ticarcillin or mezlocillin against nosocomial bloodstream isolates. *J Antimicrob Chemother.* 1986; 18:550-552.

155. Morrison AJ Jr, Freer CV, Poole CL, Johnston DO, Westervelt F Jr, Normansell DE, Wenzel RP. Prevalence of human T-lymphotropic virus Type III antibodies among patients in dialysis programs at a university hospital. *Ann Intern Med.* 1986; 104:805-807.

156. Morrison AJ Jr, Wenzel RP. Nosocomial urinary tract infections due to enterococcus: 10 years - experience at a university hospital. *Arch Intern Med.* 1986; 146:1549-1553.

157. Wenzel RP. Epidemics - identification and management. *Prevention and Control of Nosocomial Infections.* RP Wenzel, ed. Baltimore, Md: Williams & Wilkins; 1987:94-108.

158. Wenzel RP. Infection control committee meeting. *Prevention and Control of Nosocomial Infections.* RP Wenzel, ed. Baltimore, Md: Williams & Wilkins; 1987:109-115.

159. Morrison AJ, Freer CV, Searcy MA, Landry SM, Wenzel RP. Nosocomial bloodstream infections: secular trends in a statewide surveillance program in Virginia. *Infect Control*. 1986; 7(11):550-553.

160. Morrison AJ Jr, Kaiser DL, Wenzel RP. A measurement of the efficacy of nosocomial infection control using the 95 percent confidence interval for infection rates. *Am J Epidemiol*. 1987; 126:292-297.

161. Morrison AJ Jr, Hunt E, Atuk NO, Schwartzman JD, Wenzel RP. Rabies pre-exposure prophylaxis using intradermal human diploid cell vaccine: immunologic efficacy and cost-effectiveness in a university medical center and a review of selected literature. *Am J Med Sci*. 1987; 293:293-297.

162. Guenthner SH, Hendley JO, Wenzel RP. Gram negative bacilli as nontransient flora on the hands of hospital personnel. *J Clin Microbiol*. 1987; 25:488-490.

163. Wenzel RP. Prevention and treatment of hospital-acquired infections. *Cecil Textbook of Medicine.* 18th Edition. Philadelphia, Pa: W.B. Saunders Co.;1988:1541-1549.

164. Wenzel RP. Importance of antiseptics and disinfectants to the hospital epidemiologist. *Chemical Germicides in the Health Care Field: Current Status and Evaluation of Efficacy and Research Needs.* MS Favero, DHM Gröschel, eds. Arlington, Va: American Society for Microbiology; 1987:105-109.

165. Goosens H, Ghysels G, Van Laethem Y, De Wit S, Levy J, De Mol P, Clumeck N, Butzler JP, Wenzel RP. Predicting gentamicin resistance from annual usage in hospital. *Lancet*. 1986; 2:804-805.

166. Wenzel RP. Old wine in new bottles (editorial). *Infect Control*. 1986; 7:485-486.

167. Wenzel RP. Methicillin-resistant *S. aureus* and *S. epidermidis* strains: modern hospital pathogens. *Infect Control*. 1986; 7:118-119.

168. Wenzel RP. Control of infection on the two sides of the Atlantic. (editorial). *J Hosp Infect*. 1987; 9:207-210.

169. Stillman RI, Wenzel RP, Donowitz L. Emergence of coagulase negative staphylococci as major nosocomial bloodstream pathogens. *Infect Control*. 1987; 8:108-112.

170. Donowitz LG, Haley CE, Gregory WW, Wenzel RP. Neonatal intensive care unit bacteremia: emergence of gram positive bacteria as major pathogens. *Am J Infect Control*. 1987; 15:141-147.

171. Miller PJ, Searcy MA, Kaiser DL, Wenzel RP. The relationship between surgeon experience and endometritis after cesarean section. *Surg Gynecol Obstet*. 1987; 165:535-539.

172. Doebbeling BN, Wenzel RP. The epidemiology of *Legionella pneumophila* infections. *Semin Resp Infect.* 1987; 2:206-221.

173. Wenzel RP. Surveillance, the Instrument of Infection Control. *Proceedings of the National Infection Control Conference.* Mexico City, July 1987.

174. Williams J, Wenzel RP. Coping with methicillin- resistant *S. aureus* infections. measures to prevent introduction and control spread of infection. *J Crit Illness*. 1987; 2:65-68.

175. Miller PJ, Wenzel RP. Etiologic organisms as independent predictors of death and morbidity associated with bloodstream infections. *J Infect Dis*. 1987;156:471-477.

176. Wenzel RP. Towards a global perspective of nosocomial infections. *Eur J Clin Microbiol*. 1987; 6:341-343.

177. Wenzel RP. The mortality of hospital-acquired bloodstream infections: need for a new vital statistic? a) *Trans Am Clin Climatol Assoc.* 1986; 98:43-48. b) *Int J Epidemiol*. 1988; 17:225-227.

178. Pfaller MA, Wenzel RP. Coagulase-negative staphylococci. *Hospital Acquired Infection in the Pediatric Patient.* LG Donowitz, ed. Baltimore, MD: Williams & Wilkins; 1988:263-270.

179. Hoffmann KK, Western S, Kaiser DL, Wenzel RP, Gröschel DHM. Bacterial colonization and phlebitis-associated risk with transparent polyurethane film for peripheral intravenous site dressings. *Am J Infect Control*. 1988; 16:101-106.

180. Fagel DG, Wenzel RP. Vascular catheter-related infections. *Intern Med*. 1988;9:198-204

181. Wenzel RP, Carlson BB. Hospital epidemiology: beyond infection control and toward quality assurance. *Clin Microbiol Newsletter*. 1988;10:60-62.

182. Wenzel RP, Schaffner W. A new affiliation, a new name, and new directions (editorial). *Infect Control Hosp Epidemiol*. 1988;9:7.

183. Helms CM, Massanari RM, Wenzel RP, Pfaller MA, Moyer NP, Hall N. Legionnaires' disease associated with a hospital water system: a 5-year progress report on continuous hyperchlorination. *JAMA*. 1988;259:2423-2427.

184. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Hospital acquired candidemia: the attributable mortality and excess length of stay. *Arch Intern Med*. 1988;148:2642-2647.

185. Doebbeling BN, Pfaller MA, Houston AK, Wenzel RP. Removal of nosocomial pathogens from the contaminated glove: implications for glove reuse and handwashing. *Ann Int Med.* 1988;109:394-398.

186. Wenzel RP. Interaction of man and microbe: implications of the AIDS epidemic for hospital epidemiology. *Am J Infect Control*. 1988;16:214-220.

187. Martin MA, Bock MJ, Pfaller MA, Wenzel RP. Respiratory syncytial virus infections in adult bone marrow transplant recipients. *Lancet*. 1988;1:1396-1397.

188. Wenzel RP. Hospital-acquired bloodstream infections: new complications of central venous catheters. *Cur Opin in Infect Dis.* 1988;1:751-754.

189. Sullivan DH, Wenzel RP. Infections in the Nursing Home Patient. *Infections in the Elderly*. B Cunha, ed. London: John Wright; 1988:285-302.

190. Ayliffe GAJ, Wenzel RP. Nosocomial infections: overview. *Cur Opin in Infect Dis*. 1988;1:719-721.

191. Wenzel RP. Is there infection control without surveillance? *Chemotherapy*. 1988;34:548-552.

192. Doebbeling BN, Ishak MA, Wade BH, Pasquale MA, Gerszten RE, Gröschel DHM, Kadner RJ, Wenzel RP. Nosocomial *Legionella micdadei* pneumonia: 10 years experience and a case-control study. *J Hosp Infect*. 1989;13:289-298.

193. Leu HS, Kaiser DL, Mori M, Woolson RF, Wenzel RP. Hospital acquired pneumonia: attributable mortality and morbidity. *Am J Epidemiol*. 1989;129:1258-1267.

194. Wenzel RP, Streed SA. Surveillance and use of computers in hospital infection control. *J Hosp Infect.* 1989;13:217-229.

195. Martin MA, Pfaller MA, Wenzel RP. Coagulase-negative staphylococcal bacteremia: mortality and hospital stay. *Ann Intern Med*. 1989;110:9-16.

196. Pfaller MA, Wey SB, Gerarden T, Houston A, Wenzel RP. Susceptibility of nosocomial isolates of Candida species to LY121019 and other antifungal agents. *Diagn Microbiol Infect Dis*. 1989;12:1-4.

197. Martin MA, Pfaller MA, Rojas PB, Woolson RF, Wenzel RP. In vitro susceptibility of nosocomial gram negative bloodstream pathogens to quinolones and other antibiotics a statistical approach. *J Antimicrob Chemother*. 1989;23:353-361.

198. Wenzel RP. Organization for infection control. *Principles and Practices of Infectious Diseases*. 3rd Edition. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley and Sons; 1989.

199. Doebbeling BN, Wenzel RP. Nosocomial viral hepatitis. *Principles and Practices of Infectious Diseases.* 3rd Edition. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley and Sons; 1989.

200. Streed SA, Wenzel RP. Isolation. *Principles and Practices of Infectious Diseases*. 3rd Edition. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley and Sons; 1989.

201. Martin MA, Wenzel RP. Disinfection, sterilization, and disposal of infectious waste. *Principles and Practices of Infectious Diseases*. 3rd Edition. GL Mandell, RG Douglas, JE Bennett, eds. New York, NY: John Wiley and Sons; 1989.

202. Martin MA, Pfaller MA, Massanari RM, Wenzel RP. Use of cellular hydrophobicity, slime production, and species identification markers for the clinical significance of coagulase-negative staphylococcal isolates. *Am J Infect Control*. 1989;17:130-135.

203. Levy J, Van Laethem Y, Verhaegen G, Perpete C, Butzler JP, Wenzel RP. Contaminated enteral nutrition solutions as a cause of nosocomial bloodstream infection: a study using plasmid fingerprinting. *JPEN*. 1989;13:228-234.

204. Stanley GL, Pfaller MA, Mori M, Wenzel RP. Nosocomial gram-negative bloodstream isolates: A comparison of in vitro antibiotic potency. *J Hosp Infect*. 1989;14:217-225.

205. Pfaller MA, Barrett M, Koontz FP, Wenzel RP, Cunningham MD, Rollins N, Darveau RP. Clinical evaluation of a direct fluorescent monoclonal antibody test for the detection of *Pseudomonas aeruginosa* in blood cultures. *J Clin Microbiol*. 1989; Mar:558-560.

206. Doebbeling BN, Bale MJ, Koontz FP, Helms CM, Wenzel RP, Pfaller MA. Prospective evaluation of the Gen-Probe assay for detection of Legionellae in respiratory specimens. *Eur J Clin Microbiol Infect Dis.* 1989;7:748-752.

207. Pfaller MA, Gerarden T, Yu M, Wenzel R. Influence of in vitro susceptibility testing conditions on the anti-candidal activity of LY121019. *Diagn Microbiol Infect Dis*. 1989;11:1-9.

208. Wenzel RP. Hospital-acquired pneumonia: overview of the current state of the art for prevention and control. *Eur J Clin Microbiol.* 1989;8:56-60.

209. Doebbeling BN, Wenzel RP. Spontaneous streptococcal gangrenous myositis: survival with early debridement. *South Med J.* 1989;82:900-902.

210. Pfaller M, Hollis R, Johnson W, Massanari R, Helms C, Wenzel R, Hall N, Moyer N, Joly J. The application of molecular and immunologic techniques to study the epidemiology of Legionella pneumophila serogroup 1. *Diagn Microbiol Infect Dis*. 1989;12:295-302.

211. Nafziger D, Wenzel RP. Coagulase-negative staphylococci: epidemiology, evaluation and therapy. *Infectious Disease Clinics of North America*. Weber D, Rutala W, eds. Philadelphia, Pa: W.B. Saunders Company; 1989;3:915-929.

212. DeGroote MA, Martin MA, Densen P, Pfaller MA, Wenzel RP. Plasma tumor necrosis factor levels in patients with presumed sepsis results in those treated with antilipid A antibody vs. placebo. *JAMA*. 1989;262:249-252.

213. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Risk factors for hospital acquired candidemia: a matched case-control study. *Arch Intern Med.* 1989;149:2349-2353.

214. Pfaller MA, Gordee R, Gerarden T, Yu M, Wenzel RP. Fungicidal activity of cilofungin (LY121019) alone and in combination with anticapsin or other antifungal agents. *Europ J Clin Microbiol Infect Dis*. 1989;8:564-567.

215. Brown E, Wenzel RP, Hendley JO. Exploration of the microbial anatomy of normal human skin by using plasmid profiles of coagulase-negative staphylococci: search for the reservoir of resident skin flora. *J Infect Dis*. 1989;160:644-650.

216. Rasley D, Wenzel RP, Massanari RM, Streed S, Hierholzer WJ. Organization and operation of the hospital-infection-control program of the University of Iowa Hospitals and Clinics. *Infection*. 1988;16:373-378.

217. Cabezudo I, Pfaller M, Bale M, Wenzel R. In vitro comparison of cefpirome and four other beta-lactam antibiotics alone and in combination with tobramycin against clinical isolates of *Pseudomonas aeruginosa. Diagn Microbiol Infect Dis*. 1989;12:337-341.

218. Cabezudo I, Pfaller M, Gerarden T, Koontz F, Wenzel R, Gingrich R, Heckman K, Burns CP. Value of the cand-tec Candida antigen assay in the diagnosis and therapy of systemic candidiasis in high risk patients. *Eur J Clin Microbiol Infect Dis*. 1989;Sept:770-777.

219. Garibaldi R, Wenzel RP. New challenges and controversies. *Infect Control Hosp Epidemiol*. 1989;10:239.

220. Landry SL, Kaiser DL, Wenzel RP. Hospital stay and mortality attributed to nosocomial enterococcal bacteremia: a controlled study. *Am J Infect Control*. 1989;17:323-329.

221. Wenzel RP, Nettleman M. Smallpox vaccination for investigators using vaccinia recombinants. *Lancet*. 1989;2:630-631.

222. Massanari RM, Wenzel RP. Hospital infection control. *Internal Medicine*. 3rd Edition. JH Stein, ed. Boston, Mass: Little Brown & Company; 1990:1219-1225

223. Broderick A, Mori M, Nettleman MD, Streed SA, Wenzel RP. Nosocomial infections: validation of surveillance and computer modeling to identify patients at risk. *Am J Epidemiol*. 1990;131:734-742.

224. Doebbeling BN, Pfaller MA, Kuhns KR, Massanari RM, Behrendt DM, Wenzel RP. Cardiovascular surgery prophylaxis: a randomized, controlled comparison of Cefazolin and Cefuroxime. *J Thorac Cardiovasc Surg*. 1990;99:981-989. 224.

225. Tobacman J, Wenzel RP. Clinical epidemiology: further consideration. *J Clin Epidemiol*. 1990;43:633-635.

226. Wenzel RP. Quality assessment - an emerging component of hospital epidemiology. *Diagn Microbiol Infect Dis*. 1990;13:197-204.

227. Reagan DR, Nafziger DA, Wenzel RP. Handfishing-associated Klebsiella bloodstream infection. *J Inf Dis*. 1990;161:155-156.

228. Veach LA, Pfaller MA, Barrett M, Wenzel RP. Vancomycin resistance in *Staphylococcus haemolyticus* causing colonization and bloodstream infection. *J Clin Microbiol*. 1990;28:2064-2068.

229. Reagan DR, Pfaller MA, Hollis RJ, Wenzel RP. Characterization of the sequence of colonization and nosocomial candidemia using DNA fingerprinting and a DNA probe. *J Clin Microbiol.* 1990;28:2733-2738.

230. Doebbeling BN, Wenzel RP. The direct cost of universal precautions in a teaching hospital. *JAMA*. 1990;264:2083-2087.

231. Perl TM, Pfaller MA, Houston A, Wenzel RP. Effect of serum on the in-vitro activity of eleven broad-spectrum antibiotics. *Antimicrob Agents Chemother*. 1990;34:2234-2239.

232. Doebbeling BN, Pfaller MA, Bale MJ, Wenzel RP. Comparative in vitro activity of the new quinolone sparfloxacin (CI-978, AT-4140) against nosocomial gram-negative bloodstream isolates. *Eur J Clin Microbiol Infect Dis*. 1990;9:298-301.

233. Nafziger DA, Wenzel RP. Catheter-related infections: reducing the risk--and the consequences. *J Crit Ill*. 1990;5:857-863.

234. Nafziger DA, Wenzel RP. Techniques for catheter removal and culture. *J Crit Ill.* 1990;5:867-871.

235. Tucker RM, Swanson S, Salata RA, Wenzel RP. Cytomegalovirus and appendiceal perforation in the acquired immunodeficiency syndrome: a case report and review of the literature. *South Med J*. 1989; 82:1056-1057.

236. Cabezudo I, Pfaller MA, Barrett M, Bale M, Wenzel RP. In vitro comparison of mezlocillin and piperacillin plus tobramycin or gentamicin versus 100 gram-negative nosocomial bloodstream isolates. *Am J Infect Control*. 1990;18:250-256.

237. Wenzel RP, Maki DG, Crow S, Schaffner W, McGowan JE. Duplicate publication of a manuscript. *Infect Control Hosp Epidemiol*. 1990;11:341-342.

238. Pfaller MA, Cabezudo I, Hollis R, Huston B, Wenzel RP. The use of biotyping and DNA fingerprinting in typing *Candida albicans* from hospitalized patients. *Diagn Microbiol Infect Dis*. 1990;13:481-489.

239. Doebbeling BN, Wenzel RP. Prevention of Respiratory Diseases. *Respiratory Diseases in the Immunocompromised Host.* 1st edition. Shelhamer J, Pizzo PA, Parrillo JE, Masuo H, eds. New York, NY: JB Lippincott; 1991:741-759.

240. Pannuti C, Gingerich R, Pfaller MA, Wenzel RP. Nosocomial pneumonia in adult patients undergoing bone marrow transplantation: a nine year study. *J Clin Oncol.* 1991;9:77-84.

241. Wenzel RP. The development of academic programs for quality assessment. *Arch Intern Med.* 1991;151:653-654.

242. Reagan DR, Doebbeling BN, Pfaller MA, Sheetz CT, Houston AK, Hollis RJ, Wenzel RP. Elimination of coincident *Staphylococcus aureus* nasal and hand carriage with intranasal application of mupirocin calcium ointment. *Ann Intern Med*. 1991;114:101-106.

243. Cohen MB, Zaleski MS, Wenzel RP. AIDS-related safety issues for the cytology laboratory. *Diagn Cytopathol.* 1991;7:543-545.

244. Trilla A, Krueger WAK, Wenzel RP. Coagulase-negative staphylococci bloodstream infections in the ICU: new problems and few solutions. *Crit Care*. 1991;6:314-330.

245. Widmer AF, Pfaller MA, Wenzel RP, et al. Failure to isolate methicillin-resistant Staphylococcus aureus from stethoscopes in two hospitals with endemic strains. *Eur J Clin Microbiol Infect Dis*. 1991;10:46.

246. Wenzel RP. Epidemiology of hospital-acquired infection (Chapter 20). *Manual of Clinical Microbiology.* Washington, D.C.: American Society for Microbiology; 1991.

247. Wenzel R, Nettleman M, Jones R, Pfaller M. Methicillin-resistant *Staphylococcus aureus*: implication for the 1990s and effective control measures. *Am J Med*. 1991;91:221S-227S.

248. Wenzel RP, Pfaller MA. Candida species: emerging hospital bloodstream pathogens. *Infect Control Hosp Epidemiol*. 1991;12:523-524.

249. Wenzel RP, Pfaller MA. Infection control: the premier quality assessment program in United States hospitals. *Am J Med.* 1991;27S-31S.

250. Wenzel RP, Pfaller MA. Handwashing: efficacy vs. acceptance. A brief essay. *J Hosp Infect.* 1991;18 (suppl B):65-68.

251. Wenzel RP, Pfaller MA. Feasible and desirable future targets for reducing the costs of hospital infections. *J Hosp Infect*. 1991;18 (suppl B):94-98.

252. Wenzel RP. Historical aspects and future perspectives. *Infecciones intrahospitalarias: su Vigilancia y Control.* Ponce de Leon S, ed. National University of Mexico. 1990.

253. Grosserode M, Wenzel RP. The continuing importance of staphylococci as major hospital pathogens. *J Hosp Infect*. 1991;195:3-17.

254. Doebbeling BN, Hollis RJ, Isenberg HD, Wenzel RP, Pfaller MA. Restriction fragment analysis of a *Candida tropicalis* outbreak of sternal wound infections. *J Clin Microbiol*. 1991;29:1268-1270.

255. Wenzel RP. Infection control, bureaucracy, and the Anglo-American mission (a toast). *J Hosp Infect*. 1991:18 (suppl A):543-546.

256. Trilla A, Wenzel RP. Infecciones nosocomiales por *Staphylococcus aureus* resistentes a la meticilina. Un reto para el control de infecciones. *Enf Infec Y Microbiol*. 1991;9:193-195.

257. Hechemy KE, Fox JA, Gröschel DHM, Hayden FG, Wenzel RP. Immunoblot studies to analyze antibody to *Rickettsia typhi* group antigen in sera from patients with febrile cerebrovasculitis. *J Clin Microbiol*. 1991;29:2559-2565.

258. Greenman RL, Schein RMH, Martin MA, Wenzel RP, MacIntyre NR, Emmanuel G, Chmel H, Kohler RB, McCarthy M, Plouffe J, Russell JA, the XOMA Sepsis Study Group. A controlled clinical trial of murine monoclonal IgM antibody to endotoxin in the treatment of gram-negative sepsis. *JAMA*. 1991;266:1097-1102.

259. Doebbeling BN, Stanley GL, Sheetz CT, Pfaller MA, Houston AK, Annis L, Wenzel RP. Comparative efficacy of alternative handwashing agents in reducing nosocomial infections in intensive care units. *N Engl J Med.* 1992;327:88-93.

260. Doebbeling BN, Pfaller MA, Hollis FJ, Boyken LD, Pignatari AC, Herwaldt LA, Wenzel RP. Restriction endonuclease analysis of *Staphylococcus aureus* plasmid DNA from three continents. *Eur J Clin Microbiol Infect Dis*. 1992;11:4-8.

261. Wenzel RP. Modern perspectives the revolution in health care delivery. In: Wenzel RP, ed. *Assessing Quality Care: Perspective for Clinicians*. Baltimore, MD: Williams and Wilkins; 1992:3-16.

262. Perl TM, Haugen TH, Pfaller MA, Hollis R, Lakeman AD, Whitley RJ, Nicholson D, Wenzel RP. Transmission of Herpes simplex virus type 1 in an intensive care unit: failure of universal precautions. *Ann Intern Med*. 1992; 117:584-586.

263. Wakefield DS, Pfaller MA, Ludke RL, Wenzel RP. Methods for estimating days of hospitalization due to nosocomial infections. *Med Care*. 1992;30:373-376.

264. Pannuti C, Gingrich R, Pfaller MA, Kao C, Wenzel RP. Nosocomial pneumonia in patients having bone marrow transplant. *Cancer*. 1992;69:2653-2662.

265. Simberkoff MS, Hartgan PM, Hamilton JD, Dykin D, Gail M, Bartlett JG, Feorino P, Redfield R, Roberts R, DeMets D, Diaz E, Prtchett W, Spritz N, Wenzel RP. Ethical dilemmas in continuing a zidovudine trial after early termination of similar studies. *Controlled Clinical Trials.* 1992;14:6-18.

266. Holtz TH, Wenzel RP. Post discharge nosocomial wound infection surveillance: a brief review and commentary. *Am J Infect Control*. 1992;20:206-213.

267. Hornick DB, Schlesinger L, Wenzel RP. Resurgence of tuberculosis: update 1992. *Iowa Medicine.* 1992; October:411-414.

268. Widmer AF, Houston A, Bollinger E, Wenzel RP. A new standards for sterility testing for autoclaved surgical trays. *J Hosp Infect*. 1992;21:253-261.

269. Wenzel RP, Andriole VT, Bartlett JG, Batt MD, Bullock WE, Cobbs CG, Light B, Martin MA, Sanford J, Sandi MA. Antiendotoxin monoclonal antibodies for gram-negative sepsis: guidelines from the IDSA. *Clin Infect Dis.* 1992;14:973-976

270. Ephtimios IE, Barrett MS, Wenzel RP, Jones RN. In vitro antimicrobial activity of the penem BRL-42715 alone and in combination with ampicillin against respiratory tract pathogens. *J Antimicrob Chemother*. 1992;29:599-600.

271. Wenzel RP, Nettleman MD, Pfaller MA. Methicillin-resistant Staphylococcus aureus [Spanish]. *Enfermedades Infecciosas y Microbiologia Clinica*. 1992;3 (suppl):3-6.

272. Widmer AF, Nettleman M, Flint K, Wenzel RP. The clinical impact of culturing central venous catheters: a prospective study. *Arch Intern Med.* 1992;152:1299-1302.

270. Perl TA, Wenzel RP, Jones RN. In vitro activity of LY264826, an investigational glycopeptide antibiotic, against gram-positive bloodstream isolates and selected gram-negative bacilli. *J Antimicrob Chemother*. 1992;29:596-598.

274. Kathol RG, Wenzel RP. Natural history of symptoms of depression and anxiety during inpatient treatment on general medicine wards. *J Gen Intern Med*. 1992;7:287-293.

275. Sanchez ML, Wenzel RP, Jones RN. In vitro activity of decaplanin (M86-1410), a new glycopeptide antibiotic. *AAC*. 1992:873-875.

276. Barrett MS, Wenzel RP, Jones RN. In vitro activity of mersacidin (M87-1551), an investigational peptide antibiotic tested against gram-positive blood stream isolates. *Diagn Microbiol Infect Dis.* 1992;15:641-644.

277. Davis B, Wenzel RP. Striges scalp: bacteroides infection after an owl attack. *J Infect Dis*. 1992;165:975-976.

278. Wenzel RP. Preoperative antibiotic prophylaxis. *N Engl J Med*. 1992;236:337-339.

279. Pfaller MA, Wenzel RP. The impact of the changing epidemiology of fungal infections in the 1990s. *Eur J Clin Microbiol Infect Dis*. 1992;11:287-291.

280. Wenzel RP. Antiendotoxin monclonal antibodies a second look. *N Engl J Med*. 1992;326:1151-1153.

281. Doebbeling BN, Li N, Wenzel RP. An outbreak of hepatitis among health care workers: risk factors for transmission. *Am J Public Health*. 1993;83:1679-1984.

282. Trilla A, Nettleman MD, Hollis RJ, Fredrickson M, Wenzel RP, Pfaller MA. Restriction endonuclease analysis of plasmid DNA from methicillin-resistant *Staphylococcus aureus*: clinical application over a three-year period. *Infect Control Hosp Epidemiol*. 1993;14:29-35.

283. Ena J, Dick R, Jones R, Wenzel RP. The epidemiology of vancomycin usage in a university hospital. A 10-year study. *JAMA*. 1993;269:598-602.

284. Kandula PV, Wenzel RP. Postoperative wound infection following total abdominal hysterectomy: a controlled study of the increased duration of hospital stay and trends in postoperative wound infection. *Am J Infect Control*. 1993;21:201-204.

285. Wherry J, Pennington J, Wenzel RP. Tumor necrosis factor and the therapeutic potential of anti-TNF antibodies. *Crit Care Med*. 1993;21:S436-S440.

286. Bronsema DA, Adams JR, Wenzel RP. Secular trends in rates and etiology of nosocomial urinary tract infections in a university hospital. *J Urol.* 1993;150:414-416.

287. Wenzel RP. Beyond total quality management. *Clinical Performance and Quality Health Care.* 1993;1:43-48.

288. Pittet D, Thievent B, Wenzel RP, Li N, Gurman G, Suter PM. Importance of pre-existing comorbidities for prognosis of septicemia in critically ill patients. *Intensive Care Med*. 1993;19:265-272.

289. Wenzel RP. Management principles and infection control. In: Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. 2nd ed. Baltimore, Md: Williams and Wilkins; 1993:207-213.

290. Doebbeling BN, Breneman DL, Neu HC, Aly R, Yangco BG, Holley PH, March RJ, Pfaller MA, McGowan J Jr. Reagan DR, Wenzel RP, the Mupirocin Collaborative Study Group. Elimination of *Staphylococcus aureus* nasal carriage in Health Care Workers: Analysis of Six Clinical Trials with calcium mupirocin ointment. *Clin Infect Dis*. 1993;17:466-474.

291. Wenzel RP, Bone R, Glauser M. Tumor necrosis factor (editorial). *Crit Care Med*. 1993;21:S414.

292. Wenzel RP. Instituting health care reform and preserving quality: role of the hospital epidemiologist. *Clin Infect Dis*. 1993;17:831-834.

293. Edmond MB, Wenzel RP. Ethical considerations in the use of subliminal stimulation to improve handwashing compliance: scientific utility vs autonomy of the individual. *Infect Control Hosp Epidemiol.* 1993;14:107-109.

294. Widmer AF, Wenzel RP, Trilla A, Bale MJ, Jones RN, Doebbeling BN. Outbreak of *Pseudomonas aeruginosa* infections in a surgical intensive care unit: probable transmission via hands of a health care worker. *Clin Infect Dis.* 1993;16:372-376.

295. Wenzel RP. Preoperative antibiotic prophylaxis: brief historical note. *Infect Control Hosp Epidemiol.* 1993;14:121.

296. Wenzel RP. Our journal - a new era (editorial). *Infect Control Hosp Epidemiol*. 1993;14:12-13.

297. Wenzel RP, Rohrer J. A new journal (editorial). *Clinical Performance and Quality Health Care*. 1993;1:7.

298. Pittet D, Li N, Wenzel RP. Secondary and polymicrobial nosocomial bloodstream infections are associated with higher mortality. *Clin Microb Infect Dis.* 1993;12:813-819.

299. Ena J, Houston A, Wenzel RP, Jones RN. Trends in gram-positive bloodstream organism resistance: a seven-year audit of five glycopeptides and other drugs at a large university hospital. *J Chemother.* 1993;5:17-21.

300. Nettleman, MD, Wenzel, RP Jr. Adams JR, Wenzel RP. Epidemiology of bone fractures occurring during hospitalization. *Clinical Performance and Quality Health Care*. 1993;1:81-84.

301. Pallares R, Dick R, Wenzel R, Adams J, Nettleman M. Trends in antimicrobial utilization at a tertiary teaching hospital during a 15-year period (1978-1992). *Infect Control Hosp Epidemiol.* 1993;14:383-389.

302. Doebbeling BN, Reagan DR, Pfaller MA, Houston, AK, Hollis RJ, Wenzel RP. Long-term efficacy of short course intranasal mupirocin: a prospective cohort study. *Arch Intern Med*. 1994;154:1505-1508.

303. Pfaller MA, Wenzel RP. The role of the clinical microbiology laboratory in hospital epidemiology and infection control. In: McClatchey KD, ed. *Clinical Laboratory Medicine*. Baltimore, Md: Williams and Wilkins; 1992.

304. Edmond MB, Wenzel, RP. Isolation. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases*. 4th ed. New York, NY: Churchill Livingstone. 1994;2575-2579.

305. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. *JAMA*. 1994;271:1598-1601.

306. Wenzel RP. Epidemiology of nosocomial Candida infections. *Infect Dis Clin Practice*. 1994;3:S56-S59.

307. Massanari RM, Wenzel RP. Hospital infection control. In: Stein JH, ed. *Internal Medicine*. 4th ed. St. Louis, Mo: Mosby-Year Book, Inc.; 1994:1822-1829.

308. Villareal KM, Cook RA, Galgiani JN, Wenzel RP, Pappas PG, Pottage Jr. JC, Gallis HA, Crane LR. Comparative analysis of three antifungal susceptibility test methods against prospectively collected *Candida* species. *Diag Microbiol Infect Dis.* 1994;18:89-94.

309. Martin MA, Doebbeling BN, Li N, Gorelick KJ, Wenzel RP. Multivariate analyses of prognostic factors in patients with suspected gram-negative bacterial sepsis: a prospective multicenter study. *Clinical Performance and Quality Health Care*. 1994;2:119-128.

310. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Efficient detection and long-term persistence of methicillin-resistant *Staphylococcus aureus. Clin Infect Dis*. 1994;19:1123-1128.

311. Wenzel RP. Healthcare workers and the incidence of nosocomial infection: can treatment of one influence the other? A brief review. *J Chemother*. 1994;6 (suppl # 4):33-37.

312. Martin MA, Wenzel RP. Sterilization , disinfection, and disposal of infectious waste. In: Mandell, ed. *Principles and Practices of Infectious Diseases*. 1994;2579-2586.

313. Wenzel RP, Kunin CM. Should prescription antibiotics become over-the-counter drugs? *J Infect Dis.* 1994;170:1256-1257.

314. Wenzel PR. Candida bloodstream infection. In: Seifert H, ed. *Infection Control in the Immunocompromised Host.* Berlin: Blackwell Wissenschaftsverlag. 1994;109-112.

315. Wenzel RP. Hantavirus (letter). *N Engl J Med*. 1994;331:547-548.

316. Rangel-Frausto MS, Houston A, Bale M, Fu C-M, Wenzel RP. An experimental model of Candida survival and transmission in human volunteers. *Europ J Clin Micro Infect Dis.* 1994:13:590-595.

317. Dellinger EP, Gross PA, Barrett TL, Krause PJ, Martone WJ, McGowan JE, Sweet RL, Wenzel RP. Quality standard for antimicrobial prophylaxis in surgical procedures. *Clin Infect Dis*. 1994;18:422-427.

318. Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE, Sweet RL, Wenzel RP. Quality standard for the treatment of bacteremia. *Clin Infect Dis*. 1994;18:428-430.

319. Krause PJ, Gross PA, Barrett TL, Dellinger EP, Martone WJ, McGowan JE, Sweet RL, Wenzel RP. Quality standard for assurance of measles immunity among health care workers. *Clin Infect Dis*. 1994;18:431-436.

320. Edmond MB, Wenzel RP. Organization for infection control. In: Mandell, G.L., ed. *Principles and Practices of Infectious Diseases.* New York: Churchill-Livingston; 1994;2572-2575.

321. Doebbeling BN, Wenzel RP. Nosocomial viral hepatitis and infections transmitted by blood and blood products. In: Mandell, G.L., ed. *Principles and Practices of Infectious Diseases*. New York: Churchill-Livingston; 1994;2616-2632.

322. Voss A, Hollis RJ, Pfaller MA, Wenzel RP, Doebbeling BN. Investigation of the sequence of colonization and candidemia in non-neutropenic patients. *J Clin Microbiol*. 1994;32:975-980.

323. Wenzel RP, Rohrer JE. The iron triangle of health care reform. *Clinical Performance and Quality Health Care*. 1994;2:7-9.

324. Wenzel RP. A new hantavirus in North America. *N Engl J Med*. 1994;330:1004-1005.

325. Gross PA, Barrett TL, Dellinger EP, Krause PJ, Martone WJ, McGowan JE, Sweet RL, Wenzel RP. Purpose of quality standards for infectious diseases. *Clin Infect Dis*. 1994;18:421.

326. Wenzel RP. The return of tuberculosis. In: Seifert H, ed. *Infection Control in the Immunocompromised Host.* Berlin: Blackwell Wissenschaftsverlag. 1994.

327. Pittet D, Rangel-Fausto S, Li N, Tarara D, Costigan M, Rempe L, Jebson P, Wenzel RP. Systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock: incidence, morbidities and outcomes in surgical ICU patients. *Intensive Care Med* 1995;21:302-309.

328. Wenzel RP. The specialist versus the generalist. *Clinical Performance and Quality Health Care*. 1995;3:219-220.

329. Young LS, Wenzel RP. New immunotherapies for sepsis. *Proceedings of the Association of American Physicians.* 1995;107:361-364.

330. Plum G, Wenzel RP. Die epidemiologie der multiresistenten tuberculose in den vereinigten staaten von America. *Internist* 1995;36:980-986.

331. Pittet D, Wenzel RP. Nosocomial bloodstream infection: Secular trends in rates and mortality in a tertiary health care center. *Arch Intern Med.* 1995;155:1177-1184.

332. Perdreau-Remington F, Stefanik D, Peters G, Ruckdeschel G, Haas F, Wenzel R, Pulverer G. Methicillin-resistant Staphylococcus haemolyticus on the hands of health care workers: a route of transmission or a source? *J Hosp Infect*. 1995;31:195-203.

333. Wiblin RT, Wenzel RP. Infection control for oncology. In: Klastersky J, ed. *Infectious Complications of Cancer*. Kluwer Academic Publishers; 1995;83-100.

334. Reagan DR, Pfaller MA, Hollis RS, Wenzel RP. Evidence of nosocomial spread of Candida albicans causing bloodstream infection in a neonatal intensive care unit. *Diagn Microbiol Infect Dis.* 1995;21:191-194.

335. Wenzel RP. Control of antibiotic-resistant organisms (editorial) (Thailand). *J Infect Dis*. 1995;12:47-48.

336. Herwaldt LA, Wenzel RP. Dynamics of hospital-acquired infection. In*: Manual of Clinical Microbiology.* Murray PR, et al, eds. Washington DC: ASM Press. 1995:169-181.

337. Rangel-Frausto MS, Pittet D, Costigan M, Chichelly F, Happel R, Tarara D, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS): a prospective study. *JAMA*. 1995; 273(2):117-123.

338. Abraham E, Wunderink R, Silverman H, Perl TM, Nasraway S, Levey H, Bone R, Wenzel RP, Balk R, Allred R, Pennington JE, Wherry JC, and the TNF Alpha MAb Sepsis Study Group. Efficacy and safety of monoclonal antibody to human tumor necrosis factor alpha in patients with the sepsis syndrome: a controlled, randomized, double-blind, multi-center clinical trial. *JAMA*. 1995;273:934-941.

339. Wenzel RP. The hospital epidemiologist: practical ideas. *Infect Control Hosp Epidemiol*. 1995;16:166-169.

340. Perl TM, Dvorak L, Hwang T, Wenzel RP. Long-term survival and function after suspected gram-negative sepsis. *JAMA.* 1995; 274:338-345.

341. Hollis RJ, Barr J, Doebbeling BN, Pfaller MA, Wenzel RP. Familial carriage of methicillin-resistant Staphylococcus aureus and subsequent infection in a newborn sibling. *Clin Infect Dis.* 1995;21:328-332.

342. Wenzel RP, Perl T. The significance of nasal carriage of *Staphylococcus aureus* and the incidence of postoperative wound infection*. J Hosp Infect*. 1995;31:13-24.

343. Wenzel RP. Nosocomial candidemia: Risk factors and attributable mortality*. Clin Infect Dis*. 1995;20:1531-1534.

344. Edmond MB, Ober JF, Weinbaum DL, Sanford MD, Pfaller MA, Hwang T, Wenzel RP. Vancomycin-resistant *Enterococcus faecium* bacteria: risk factors for infection. *Clin Infect Dis*. 1995;20:1126-1133.

345. Edmond MB, Hollis RJ, Houston AK, Wenzel RP. Molecular epidemiology of an outbreak of meningococcal disease in a university community. *J Clin Microbiol.* 1995;33:2209-2211.

346. Pfaller MA, Wendt C, Hollis RJ, Wenzel RP, Fritschel SJ, Neubauer JJ, Herwaldt LA. Comparative evaluation of an automated ribotyping system versus pulsed-field gel electrophoresis for epidemiological typing of clinical isolates of *Escherichia coli* and *Pseudomonas aeruginosa* from pateints with recurrent gram-negaive bacteremia. *Diagn Microbiol Infect Dis* 1996;25:1-8.

347. Wenzel RP. The economics of nosocomial infection. Lowbury Lecture for 1994. *J Hosp Infect.* 1995;31:79-87.

348. Goldmann DA, Weinstein RA, Wenzel RP, Tablan OC, Duma RJ, Gaynes RP, Schlosser J, Martone MJ. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals - a challenge to hospital leadership. *JAMA.* 1996;275:234-240.

349. Bone RC, Balk RA, Fein AM, Perl TM, Wenzel RP, Reines D, Quenze RW, Iberti TJ, Macintyre N, Schein RM, The E5 Sepsis Study Group. A second large controlled clinical study of E5, a monoclonal antibody to endotoxin: results of a prospective, multicenter, randomized, controlled trial. *Crit Care Med*. 1996;23:994-1006.

350. Edmond MB, Wenzel RP, Pasculle AW. Vancomycin-resistant *Staphylococcus aureus*: perspectives on measures needed for control. *Ann Intern Med*, 1996;124:329-334.

351. Mathers WD, Sutphin JE, Folberg R, Meier PA, Wenzel RP, Elgin RG. Outbreak of keratitis presumed to becaused by Acanthamoeba. *Amer J Ophthalmol.* 1996;121:129-142.

344. Wiblin RT, Wenzel RP. Hospital-acquired pneumonia.in *Current Topics in Infectious Diseases,* Remington JS, Swartz MN, eds. Blackwell Science, 1996.Volume 16, 194-214.

353. Wenzel RP. Airline travel and infection. *N Engl J Med.* 1996;334:981-982.

354. Edmond MB, Ober JF, Dawson JD, Weinbaum DL, Wenzel RP. Vancomycin-resistant Enterococcal bacteremia: natural history and attributable mortality. *Clin Inf Dis* 1996;23:1234-1239.

355. Wenzel RP. Total quality management: An epidemiologist s frank perspective. *Clinical Performance and Quality Health Care.* 1996;4:115-117.

356. Flanagan JR, Pittet D, Li N, Thievent B, Suter PM, Wenzel RP. Predicting survival of patients with sepsis by use of regression and neural network models. *Clinical Performance and Quality Health Care* 1996;4:96-103.

357. Pittet D, Thievent B, Wenzel RP, Li N, Auckenthaler R, Suter PM. Bedside prediction of mortality from bacteremic sepsis. A dynamic analysis of ICU patients. *Am J Respir Crit Care Med* 1996; 153:684-693.

358. Waggoner-Fountain LA, Walker MW, Hollis RJ, Pfaller MA, Ferguson JE, Wenzel RP, Donowtiz LG. Vertical and horizontal transmission of unique *candida* species to premature newborns. *Clin Infect Dis*. 1996;22:803-808.

359. Wright WL, Wenzel RP. Nosocomial Candida: epidemiology, transmission, and prevention. *Inf Dis Clinics of N Amer*. 1997;11:411-425.

360. Classen DC, Burke JP, Wenzel RP. Infectious Diseases Consultation: Impact on outcomes for hospitalized patients and results of a preliminary study. *Clin Infect Dis.*1997;24:468-70

361. Rohrer JE, Vaughan M, Wenzel RP. Regionalization of tertiary care: Impact of safe cardiovascular volumes in Iowa. *Health Services Management Research*. 1997;10:1-6.

362. Pittet D, Li N, Woolson RF, Wenzel RP. Microbiological factors influencing the outcome of nosocomial bloodstream infections: a six-year validated, population-based model. *Clin Infect Dis.*1997; 24: 1068-1078.

363. Wenzel RP. Health care reform and the hospital epidemiologist. In: RP Wenzel, ed. *Prevention and Control of Nosocimial Infections*. 3rd ed. Baltimore, Md: Williams and Wilkins; 1997. pp.47-54.

364. Rangel-Frausto MS, Wenzel RP. The epidemiology and natural history of bacterial sepsis. In: Fein AM, ed. Sepsis in multiorgan failure: Mechanisms for treatment strategies. Baltimore, Md: Williams and Wilkins; 1997, pp.27-34.

365. Lundberg JS, Perl TM, Wiblin RT, Costigan MD, Dawson J, Nettleman MD, Wenzel RP. Septic shock: an analysis of management on wards versus intensive care units. *Crit Care Med.*1998; 26(6):1020-1024.

366. Rangel-Frausto MS, Rhomberg P, Hollis R, Pfaller MA, Wenzel RP, Helms CM, Herwaldt LA. Persistance of Legionella pneumophila in a hospital's water system: A 13 year survey. *Infect Control Hosp Epidemiol* 1999 Dec; 20(12): 793-7

367. Massanari RM, Wenzel RP. Hospital infection control. In: Stein JH ed. Internal Medicine. 5th ed. 1998: St.Louis, MO., Mosby-Year Book, Inc. pp.1361-66.

368. Wenzel RP. Introduction: The infectious diseases specialist in the late 1990s. *Clin Infect Dis* 1997; 24(3):456

369. Wendt C, Messer SA, Hollis RJ, Pfaller MA, Wenzel RP, Herwaldt LA. Molecular epidemiology of recurrent gram-negative bacteremia. *Clin Inf Dis* 1999; 28: 605-10

370. Lundberg J, Costigan M, Bentler S, Dawson J, Nettleman M, Wenzel RP. *Staphylococcus aureus* bacteremia: The effect of an infectious diseases consultation on patient outcome. *Clin Perf and Quality Health Care* 1998; 6: 9-11.

371. Wenzel RP, Reagan DR, Bertino JS, Baron EJ, Arias K. Methicillin-resistant *Staphylococcus aureus* outbreak: A consensus panel s definition and management guidelines. *Amer J Infect Control* 1998; 26:102-110.

372. Diekema DJ, Messer SA, Hollis RJ, Wenzel RP, Pfaller MA. An outbreak of *Candida parapsilosis* prosthetic valve endocarditis. *Diagn Microbiol Infect Dis* 1997; 29: 147-153.

373. Herwaldt LA, Swartzendruber SK, Edmond MB, Embrey RP, Wilkerson KR, Wenzel RP, Perl TM. The epidemiology of hemorrhage related to cardiothoracic operations. *Infect Control & Hosp Epidemiol* 1998; 1: 9-16.

374. Pittet D, Davis CS, Li N, Wenzel RP. Identifying the hospitalized patient at risk for nosocomial bloodstream infection: a population-based study. *Proceedings of the Association of American Physicians*. 1997;109:58-67.

375. Meier PA, Mathers WD, Sutphin JE, Folberg R, Hwang T, Wenzel RP. An epidemic of presumed Acanthamoeba Keratitis that followed regional flooding: results of a case-control investigation. *Arch Ophth* 1998; 116(8): 1090-4.

376. Wenzel RP. The Hospital Epidemiologist: Practical Ideas. In A Practical Handbook for Hospital Epidemiologists.1998, Slack Inc., pp. 7-12.

377. Wenzel RP, Edmond MB. The Evolving Technology of Venous Access. *N Engl J Med* 1999; 340: 48-49.

378. Wenzel RP, Pinsky MR, Ulevitch RJ, Young LS. Current understanding of sepsis. *Clin Infect Dis.* 1996;22:407-413.

379. Perdreau-Remington F, Stefanik D, Peters G, Ludwig C, Rutt J, Wenzel RP, Polverer G. A 4-year prospective study on microbial ecology of explanted prosthetic hips in 52 patients with aseptic prosthetic joint loosening. *E J Clin Microbiol Infect Dis*. 1996;15:160-165.

380. Wenzel RP, Nettleman MD. Principles of Hospital Epidemiology. In *Hospital Epidemiology and Infection Control*, CG Mayhall, ed., Baltimore, MD: Williams & Wilkins, 1996, pp.13-79.

381. Wendt C, Wenzel RP. The value of the hospital epidemiologist. *Clin Microbiology and Infect.* 1996; 1:154-9.

382. Wenzel RP, Edmond MB, Nettleman MD. Hospital Epidemiology - 1997. *Virginia Medical Quarterly*, 1997;2:103-104.

383. Bischoff WE, Reynolds TM, Sessler CN, Edmond MB, Wenzel RP. Handwashing Compliance by Health Care Workers: The Impact of Introducing an Accessible, Alcohol-based Hand Disinfectant. *Arch Int Med* 2000; 160: 1017-1021.

384. Pfaller MA, Jones RN, Marshall SA, Coffman SL, Edmond MB, Wenzel RP. Inducible Amp C -lactamase producing gram-negative bacilli from blood stream infections: Frequency, antimicrobial susceptibility and molecular epidemiology in a national surveillance program (SCOPE). *Diagn Microbiol Infect Dis* 1997; 28: 211- 219

385. Rangel-Frausto SM, Pittet D, Hwang T, Woolson RF, Wenzel RP. The Dynamics of Disease Progression in Sepsis: Markov Modeling Describing the Natural History and the Likely Impact of Effective Anti-Sepsis Agents.*Clin Inf Dis* 1998; 27: 185-90.

386. Wilke WW, Marshall SA, Coffman SL, Pfaller MA, Edmond MB, Wenzel RP, Jones RN. Vancomycin-resistant *Enterococcus raffinosus:* Molecular epidemiology, species identification error and frequency of occurrence in a national resistance surveillance program. *Diagn Microbiol Infect Dis* 1997; 28.

RPW bibl

387. Jones RN, Marshall SA, Pfaller MA, Wilke WW, Hollis RJ, Erwin ME, Edmond MB, Wenzel RP, and the SCOPE Hospital Study Group. Nosocomial Entococcal Blood Stream Infections in the SCOPE Program: Antimicrobial Resistance, Species Occurrence, Molecular Testing Results and Laboratory Testing Accuracy. *Diag Microbiol Infect Dis* 1997; 29: 75-102.

388. Pfaller MA, Messer SA, Houston A, Blumberg HM, Edwards JE, Jarvis W, Martin MA, Neu HC, Patterson JE, Rinaldi MG,Sailman L, Wiblin T, Wenzel RP. National Epidemiology of Mycoses Survey: A Multicenter Study of Strain Variation and Antifungal Susceptibility Among Isolates of *Candida* Species. *Diag Microbiol Infect Dis* 1998; 31: 289-96.

389. Wenzel RP, Kontos HA. Clinical Service-line Structures Can Better Carry Out the Missions of Traditional Clinical Departments *Acad Med* 1999; 10: 1055-1057.

390. Pfaller MA, Jones RN, Marshall SA, Edmond MB, Wenzel RP and the SCOPE Hospital Study Group. Nosocomial Streptococcal Blood Infections in the SCOPE Program: Species, Occurances and Antimicrobial Resistance *Diag Microbiol Infect Dis* 1997; 29: 259-263.

391. Wenzel RP, Edmond M. Tuberculosis Infection after Bronchoscopy. *JAMA*, 1997; 278:1111.

392. Pfaller MA, Jones RN, Messer SA, Edmond MB, Wenzel RP, and the SCOPE Participant Group. National Surveillance of Nosocomial Blood Stream Infection Due to Species of *Candida* Other than *Candida albicans*: Frequency of Occurrence and Antifungal Susceptibility in the SCOPE Program, 1995-96. *Diagn Microbiol Inf Dis* 1998; 30:121-129.

393. Wenzel RP, Girtman J, Costello D, Nettleman MD. Costs of Providing Primary Care. *Clin Perf Qual Health Care* 1999; 7: 43-47.

394. Pfaller MA, Jones RN, Messer SA, Edmond MB, Wenzel RP. National Surveillance of Nosocomial Blood Stream Infection Due to *Candida albicans*: Frequency of Occurrence and Antifungal Susceptibility in the SCOPE Program. *Diag Microbiol Infect Dis* 1998; 31:327-332.

395. Pfaller MA, Lockhart SR, Pujol C, Swails-Wenger JA, Messer SA, Edmond MB, Jones RN, Wenzel RP, Soll DR. Hospital Specificity, Regional Specificity and Fluconizole-Resistance of *Candida albicans* Blood Stream Isolates. *J Clin Microbiol* 1998; 36: 1518-1529.

396. Franchi D, Wenzel RP. Measuring Health-Related Quality of Life Among Patients Infected with Human Innumodeficiency Virus. *Clin Inf Dis* 1998;26:20-26.

397. Wendt C, Messer SA, Hollis RJ, Pfaller MA, Wenzel RP. Recurrent Gram-Negative Bacteremia: Incidence and Clinical Patterns. *Clin Inf Dis* 1999; 28:611-7.

398. Wenzel RP, Edmond MB. Vancomycin-Resistant *Staphylococcus aureus*: Infection Control Considerations. *Clin Inf Dis* 1998; 27:245-51.

399. Wenzel RP. Health Care Reform and the Specialist in Infectious Diseases. In Mandell G, ed. Principles and Practices of Infectious Diseases. 2000, New York: Churchill Livingstone, pp.

400. Wenzel RP. Attributable Mortality: the Promise of Better Antimicrobial Therapy. *J Inf Dis* 1998; 178: 917-9.

401. Wenzel RP. Managed Health Care: Outcomes and Update. In: Remington J., ed. Current Clinical Topics in Infectious Diseases, 1999; 19: 216-25

402. Zaidi M, Wenzel RP. Disinfection, Sterilization, and Control of Hospital Waste. In Mandell G, ed. Principles and Practices of Infectious Diseases. 2000, New York: Churchill Livingstone, pp.2995-3005.

403. Wiblin T, Wenzel RP. The Infection Control Committee. In Herwaldt LA, Decker MD., eds. A Practical Handbook for Hospital Epidemiologists. Slack Inc., NJ. 1998, pp.29-32

404. Retchin SM, Wenzel RP. Electronic Medical Record Systems at Academic Health Centers: Advantages and Implementation Issues. *Acad Med* 1999; 74: 493-498.

405. Rangel-Frausto S, Wiblin T, Blumberg HM, Saiman L, Patterson J , Rinaldi M, Pfaller M, Edwards JE, Jarvis W, Dawson J, Wenzel RP. National Epidemiology of Mycosis Survey (NEMIS). Variation in Rates of Candida Bloodstream Infection in Seven Surgical ICUs and Six Neonatal ICUs. *Clin Iifect Dis* 1999; 29:253-8.

406. Wenzel RP, Edmond MB. Managing Antibiotic Resistance. *N Engl J Med* 2000; 343: 1961-3

407. Wong AHM, Wenzel RP, Edmond MB. The Epidemiology of Bacteriuria with Vancomycin-Resistant Enterococci. *Amer J Infect Control* 2000; 28: 277-81

408. Wong AHM, Wenzel RP. Using Quality Improvement Techniques for the Prevention of Nosocomial Pneumonia. In Jarvis, WR ed. Nosocomial Pneumonia. Marcel Dekker, Inc. New York-Basel. 2000; pp.187-201.

409. Wenzel PR, Nettleman MD. Medicare and Outpatient Therapy of Infectious Diseases. *Clin Inf Dis* 1998;27: 1422- 3.

410. Roy M-C, Herwaldt LA, Embrey R, Kuhns K, Wenzel RP, Perl TM. Does the Centers for Disease Control's NNIS Risk Index Stratify Patients Undergoing Cardiothoracic Operations by Their Risk of Surgical Site Infection? *Infect Control Hosp Epidemiol* 2000; 3: 186-190.

411. Fätkenheuer G, Taelman H, Schwenk A, Wenzel R. The Return of Tuberculosis. *Diag Micro Infect Dis* 1999.

412. Wenzel RP, Wong M. Managing Antibiotic Use. (Editorial) *Clin Inf Dis* 1999; 28: 1126-7.

413. Edmond MB, Wallace SE, McClish DK, Pfaller MA, Jones RN, Wenzel RP. Nosocomial Bloodstream Infections in United Stated Hospitals: A Three-Year Analysis. *CID* 1999; 29: 239-44.

414. Saiman L, Ludington E, Pfaller M, Rangel-Frausto S, Wiblin RT, Dawson J, Blumberg HM, Patterson JE, Rinaldi M, Edwards JE, Martin MA, Wenzel RP. Risk Factors for Candidemia in Neonatal Intensive Care Unit Patients, Including the Role of Gastrointestinal Colonization. *Ped Inf Dis* 2000; 19: 319-24.

415. Marco F, Lockhart SR, Pfaller MA, Rangel-Frausto MS, Wiblin T, Blumberg HM, Edwards JE, Jarvis W, Martin MA, Saiman L, Petterson JE, Dibb JC, Roldan CM, Rinaldi MG, Wenzel RP, Soll DR. Elucidating the Origins of Nosocomial Infections of *Candida albicans* by DNA Fingerprinting with the Complex Probe Ca3. *J Clin Microbiol* 1999; 37: 2817-28.

416. Bischoff WE, Reynolds TM, Hall GO, Wenzel RP, Edmond MB. Molecular Epidemiology of Vancomycin-Resistant *Enterococcus faecium* (VREF) in a Large Urban Hospital over a Five-Year Period. *J Clin Microbiol* 1999; 37: 3912-16

417. Franchi D, Climo MW, Wong AHM, Edmond MB, Wenzel RP. Seeking Vancomycin Resistant *Staphylococcus aureus* Among Patients with Vancomycin-Resistant Enterococci. *Clin Inf Dis* 1999; 29: 1556-8.

418. Wong MT, Kauffman CA, Standiford HC, Fuchs HJ, Wenzel RP and the Ramoplanin-VRE 2 Clinical Study Group. Effective Suppression of Vancomycin-Resistant *Enterococcus* in Asymptomatic Gastrointestinal Carriers by a Novel Glycolipodepsipeptide, Ramoplanin. *Clin Inf Dis* 2001; 33:1476-82.

419. Edmond MB, Wenzel RP. Organization for Infection Control. In Mandell G, ed. Principles and Practices of Infectious Diseases. 2000, New York: Churchill Livingstone, pp.2889-91.

420. Edmond MB, Wenzel RP. Isolation. In Mandell G, ed. Principles and Practices of Infectious Diseases. 2000, New York: Churchill Livingstone, pp.2991-5.

421. Wenzel RP. Does Infection Control Control Infections? *Schweiz Med Wochenschr* 2000; 130:119-21.

422. Wenzel RP. Expanding the Treatment Options for Influenza. *JAMA* 2000; 283: 1057-9.

423. Wenzel R. Of Mice, Men, and Microbes: Hantavirus. (Book review). *N Engl J Med* 2000; 342: 666.

424. Wenzel RP, Edmond MB. The Impact of Hospital-Acquired Bloodstream Infections. *Emerging Infect Dis* 2001; 7: 174-7.

425. Perl TM, Cullen J, Wenzel RP et al Intranasal Mupirosin to Prevent Postoperative *S.aureus. N Engl J Med* 2002; 346: 1871-7.

426. Wenzel RP. Perspective: Treating Sepsis. *N Engl J Med* 2002; 347:966-8.

427. Blumberg HM, Wenzel RP. Risk Factors for *Candida* Bloodstream Infections in Surgical Intensive Care Unit Patients: the NEMIS Prospective Multicenter Study. *Clin Inf Dis* 2001;33:177-86.

428. Wisplinghoff H, Seifert H, Coimbra M, Wenzel RP, Edmond MB. Systemic Inflammatory Response Syndrome (SIRS) in Adult Patients with Nosocomial Bloodstream Infection due to Staphylococcus aureus. *Clin Infect Dis* 2001; 33:733-6.

429. Wenzel RP, Edmond MB. Penicillin-Resistant Pneumococcus. MD Vista Journal of Medicine. August 2000. (http://www.mdvista.com/templates/professionaleducation/article.asp?id=7339)

430. Wenzel, RP. Infection Control. *Current Inf Dis Reports* 2000; 2:485-6.

431. Wenzel, RP. Book Review. The Antibiotic Paradox: How the Misuse of Antibiotics Desttroys Their Creative Powers (Stuart Levy). *N Engl J Med* 2002; 347:1213.

432. Wisplinghoff H, Edmond MB, Pfaller MA, Jones RN, Wenzel RP, Seifert H. Nosocomial Bloodstream Infections Caused by *Acinetobacter* Species in United States Hospitals: Clinical Features, Molecular Epidemiology, and Antimicrobial Susceptibility. *Clin Inf Dis* 2000; 31: 690-7.

433. Costa ST, Ausiello D, Joiner K, Neilson EG, Taylor I, Wenzel RP. Supporting Research in Departments of Internal Medicine: Recommendations for NIH. *Am J Med* 2000; 109:178-180.

434. Saiman L, Ludington E, Dawson J, Patterson JE, Rangel-Frausto S, Wiblin RT, Blumberg HM, Pfaller M, Rinaldi M, Edwards JE, Wenzel RP, Jarvis W and the NEMIS study group. Risk Factors for colonization of neonatal intensive care unit patients with *Candida*. *Pediat Inf Dis J* 2001; 20: 1119-24.

435.Wenzel RP, Gennings C, Edmond MB. Antifungal Antibiotics and Breakthrough Bacteremias. *Clin Inf Dis* 2001; 32:1538-9.

436. Rangel-Frausto MS, Rhomberg P, Hollis RJ, Pfaller MA, Wenzel RP, Helms CM, Herwaldt LA. Persistence of Legionella pneumophila in a hospital's water system: a 13-year survey. Infect Control Hosp Epidemiol 1999 Dec; 20(12):793-7.

437. Wenzel RP, Edmond MB. Multidrug-Resistant *Streptococcus pneumoniae* (Response -in a letter) *N Engl J Med* 2001; 344:1329-31.

438. Wenzel RP. Recognizing the Real Threat of Biological Terror.*Trans of the Amer Clin and Climatolog Assoc* 2002; 113:42-55.

439. Edmond MB, McClish D, Massie TR, Wiblin T, Kauffman C, Goff D, Rex J, Schuster M, Wenzel RP. Risk Factors for Nosocomial Candidemia Among Patients in Eight Surgical Intensive Care Units. (in preparation)

440. Wenzel RP, Edmond MB. Severe Sepsis - National Estimates. *Crit Care Med* 2001; 29:1472-4.

441. Edmond MB, Deschens JL, Eckler M, Wenzel RP. Racial Bias in Using USMLE Step 1 Scores to Grant Internal Medicine Residency Interviews. Academic Medicine 2001; 76(12):1253-1256.

442. Tallent SM, Bischoff T, Climo M, Ostrowsky B, Wenzel RP, Edmond MB. Vancomycin Susceptibility of Oxacillin-Resistant Staphylococcus aureus Isolates Causing Nosocomial Bloodstream Infections. *J Clin Microbiol* 2002, 40: 2249-50.

443. Wenzel RP. A Focus on Community-Acquired Pneumonia. *Advanced Studies in Medicine* 2002; 2(4): 110-116.

444. Wenzel RP, Sahm DF, Thornsbery C, Draghi DC, Jones ME, Karnowsky J. In vitro Susceptibilities of Gram-Negative Bacteria Isolated from Hospitalized Patients in Four European Countries, Canada, and the United States in 2000-2001 to Expanded-Spectrum Cephalosporins and Comparator Antimicrobials: Implications for Therapy. *Antimicrobial Agents and Chemother* 2003; 47:3089-3098.

445. Pfaller MA, Wenzel RP. The Epidemiology of Fungal Infections. In *Clinical Mycology* EJ Anaissie, MR McGinnis, MA Pfaller, eds. Churchill Livingston; New York; 2003:pp. 3-19.

446. Wenzel RP. Bioterror. In *Prevention and Control of Nosocomial Infections.* 4th edition. RP Wenzel, ed. Baltimore. Lippincott, Williams and Wilkins; 2003.

447. Wenzel RP. Management. In *Prevention and Control of Nosocomial Infections.* 4th edition. RP Wenzel, ed. Baltimore. Lippincott, Williams and Wilkins; 2003.

448. Ostrowsky B, Ober J, Wenzel R, Edmond M. The Case of the cold thermometers. *Am J Infect Control* 2003; Feb 3; 31(1):57-9.

449. da Silva Coimbra MV, Silva-Carvalho MC, Wisplinghoff H, Hall GO, Tallent S, Wallace S, Edmond MB, Figueiredo AM, Wenzel RP. Clonal spread of methicillin-resistant *Staphylococcus aureus* in a large geographic area of the United States. *J Hosp Infect* 2003 Feb; 53(2): 103-10.

450. Wisplinghoff H, Wenzel RP. Current Trends in the epidemiology of nosocomial bloodstream infections in patients with hematological malignancies and solid neoplasms in US hospitals. *Clin Inf Dis* 2003; 36:1103-10.

451. Herwaldt LA, Cullen JJ, French P, Hu J, Pfaller MA, Wenzel RP, Perl TM. Risk factors for nasal carriage of *Staphylococcus aureus* in a large population of surgical patients. *Inf Contr Hosp Epidem* 2004:25:481-4.

452. Wenzel RP, Edmond MB. Managing SARS amidst Uncertainty. *N Engl J Med* 2003:348(20):1947-8.

453. Wenzel, RP. Introduction to antifungal prophylaxis in the surgical intensive care unit. (in press)

454. Rex JH, Wingond JR, Wenzel R, et al. The design of clinical trials that evaluate antifungal prophylaxis and combination therapy: introduction and overview. *Clin Inf Dis* 2004; 39 Suppl (S165-9)

455. Wenzel RP, Edmond MB. Listening to SARS: Lessons for Infection Control. *Ann Intern Med* 2003;139:592-93.

456. Edmond MB, Wenzel RP. Isolation. In Mandell, G. ed. Principles and Practices of Infectious Diseases , New York: Churchill Livingstone. 2005, pp.3323-5

457. Edmond MB, Wenzel RP. Organization for Infection Control In In Mandell, G. ed. Principles and Practices of Infectious Diseases, New York: Churchill Livingstone. 2005, pp.3326-8.

458. Jones ME, Draghi DC, Thornberry C, Karlowsky JN, Sahm DF, Wenzel RP. Emerging resistance among bacterial pathogens in the Intensive Care Units - a European and north American Surveillance Study (2000-2002). *Ann Clin Microbiol Antimicrob* 2004; 3:14-20.

459. Gonzalez A, Bischoff T, Tallent S, Shek G, Ostrowsky B, Edmond MB, Wenzel RP. Antibiotic resistance in the community: The Richmond ARC Project. *J Hosp Infect* 2003; 55(2): 156-7.

460. Wisplinghoff H, Seifert H, Tallent SM, Bischoff T, Wenzel RP, Edmond MB. Nosocomial Bloodstream Infections in Pediatric Patients in US Hospitals: Epidemiology, Clinical Feantures and Susceptibilities. *Pediatr Inf Dis* 2003;22:686-91

461. Harris NS, Wenzel RP, Thomas SH. High altitude headache: efficacy of acetaminophen vs ibuprofen in a randomized, controlled trial. *J Emerg Med* 2003; 24:383-7.

462. Wisplinghoff H, Bischoff T, Tallent SM, Seifert H, Wenzel RP, Edmond MB. Nosocomial Bloodstream Infections in US Hospitals: Analysis of 24,179 cases from a prospective nationwide surveillance study. *Clin Inf Dis* 2004; 39:309-17.

463. North MA, Wenzel RP. Performances and practices of successful academic practices: faculty practice plan governance. *MGMA*, 2004.

464. Wenzel RP. The Antibiotic Pipeline: challenges, costs and values. *N Engl J Med* 2004; 351:523-5.

465. Herwaldt LA, Cullen JJ, Scholz D, French P, Zimmerman MB, Pfaller MA, Wenzel RP, Perl TM. A Prospective Study of Outcomes, Health Care Utilization and Costs Associated with Postoperative Nosocomial Infections. *Inf Control Hosp Epidemiol* 2006 Dec; 27(12):1291-8.

466. Wenzel RP, Del Favero A, Kibbler C, Rogers TR, Rotstein C, Mauskopf J, Morris S, Schlamm H, Troke P, Marciniak A. Economic evaluation of voriconazole compared with amphotericin B for the primary treatment of aspergillosis in immunocompromized patients. *J Antimicrob Chemother* 2005, 55:352-61.

467. Wenzel RP, Bearman G, Edmond MB. Lessons from SARS: Implications for infection control. *Arch Med Res* 2005 Nov-Dec; 36(6):610-6.

468. Polk RE, Johnson CK, McClish D, Wenzel RP, Edmond MB. Predicting hospital rates of fluroquinolone-resistant *Pseudomonas aeruginosa* from flurioquinolone use in U.S. hospitals and their surrounding communities. *Clin Infect Dis* 2004; 39:497-503.

469. Wenzel RP, Gennings C. Candida bloodstream infections in the intensive cate unit: Identifying expecially high risk patients for prevention strategies. *Clin Inf Dis* 2005; 41:S389-93.

470. Marra AR, Bearman GML, Wenzel RP, Edmond MB. Comparison of severity of illness scoring systems for patients with nosocomial bloodstream infection due to *Pseudomonas aeruginosa*. *BMC Infect Dis*. 2006 Aug 17; 6:132.

471. Wenzel RP, Edmond MB. Patient to patient transmissions of hepatitis C. *Ann Intern Med* 2005; 142:940-41.

472. von Baum H, Ober JF, Wendt C, Wenzel RP, Edmond MB. Antibiotic-resistant nosocomial bloodstream infections: specific risk factors in a high risk population. *Infection* 2005 Oct; 33(5-6):320-6.

473. Dow A, Leong D, Anderson A, Wenzel RP and the VCU theatre-medicine team. Teaching Empathy to Medical Residents. *J Gen Intern Med* 2007; 22:1114-8; epub ahead of print, May 8.

474. Wenzel RP. Acute Tracheitis and Bronchitis. *Cecil Textbook of Medicine* (in press 2007)

475. Wenzel RP, Bate G, Kirkpatrick P. Tigecycline. *Nat Rev/Drug Discovery* 2005; 4:13-14

476. Bearman GM, Wenzel RP. Bacteremias: a leading cause of death. *Arch Med Res* 2005; 36(6):646-59.

477. Marra AR, Bar K, Bearman GM, Wenzel RP, Edmond MB. Systemic inflammatory response syndrome in adult patients with nosocomial bloodstream infection due to *Pseudomonas aeruginosa*. *J Infect* 2006; Jul; 53(1):30-50. (e-pub ahead of print Oct 25, 2005).

478. Fulco P, Wenzel RP. Ramoplanin: a topical lipoglycodepsipeptide antibacterial agent. *Expert Rev Anti Infect Ther* 2006 Dec; 4(6): 939-45.

479. Marra AR, Bar K, Bearman GM, Wenzel RP, Edmond MB. Systemic inflammatory response syndrome in nosocomial bloodstream infections with *Pseudomonas aeruginosa* and Enterococcus Species: comparison of elderly and nonelderly patients. *J Am Geriatr Soc*. 2006 May; 54(5):804-8.

480. Marra AR, Bearman GM, Wenzel RP, Edmond MB. Comparison of the systemic inflammatory response syndrome between monomicrobial and polymicrobial *Pseudomonas aeruginosa* nosocomial bloodstream infections. *BMC Infect Dis.* 2005 Oct 31; 5:94.

481. Bar K, Wisplinghoff H, Wenzel RP, Bearman GM, Edmond MB. Systemic inflammatory response syndrome in adult patients with nosocomial bloodstream infections due to enterococci. *BMC Infect Dis* 2006 Sep 26; 6:145.

482. Wisplinghoff H, Seifert H, Wenzel RP, Edmond MB. Inflammatory response and clinical course of adult patients with nosocomial bloodstream infections caused by Candida spp. *Clin Microbiol Infect.* 2006 Feb; 12(2):170-7.

483. Wenzel RP, Fowler AA 3rd. Clinical practice. Acute bronchitis. *N Engl J Med* 2006 Nov 16; 355(20):2125-30.

484. Bearman GM, Munro C, Sessler CN, Wenzel RP. Infection control and the prevention of nosocomial infections in the intensive care unit. *Semin Respir Crit Care Med*. 2006 Jun; 27(3):310-24.

485. Marra AR, Edmond MB, Forbes BA, Wenzel RP, Bearman GM. Time to blood culture positivity as a predictor of clinical outcome of Staphylococcus aureus bloodstream infection. *J Clin Microbiol* 2006 Apr; 44(4):1342-6.

486. Wenzel RP. John E. Bennett Forum on deep mycoses study design 2004: Candidiasis and salvage therapy for aspergillosis *Clin Infect Dis* 2005; 41 Suppl 6:S369-70.

487. Wenzel RP, Edmond MB. Team-based Prevention of Catheter-Related Infections. *N Engl J Med 2006*; 355:2781-3.

488. Hoopwood D, Levy S, Wenzel RP et al. A call to arms. *Nature Reviews Drug Discovery* 2007; 6:2-5.

489. Bearman GML, Marra AR, Sessler CN, Smith WR, Rosato A, Laplante JK, Wenzel RP, Edmond MB. A controlled trial of universal glowing vs. contact precautions for preventing the transmission of multidrug-resistant organisms. (submitted, 2007)

490. Wenzel RP. Healthcare associated infections: major issues in the early years of the 21 century. *Clin Inf Dis* 2007 45 Suppl 1:S85-88.

491. Wenzel RP, Bearman G, Edmond MB. Community Acquired MRSA: new issues for infection control. *Int J of Antimicrob Agents* 2007; 30:210-212.

492. Gupta S, Gennings C, Wenzel RP. R=20:Bias in the Reporting of Respiratory Rates. *Amer J Emerg Med*, accepted, 2007.

493. Marra AR, Edmond MB, Wenzel RP, Bearman GM. Hospital-acquired Clostridium difficile disease in the Intensive Care Unit Setting: Epidemiology, Clinical Course and Outcome. *BMC Infect Dis* 2007; May 21:(1) 42 [epub ahead of print].

494. Wenzel RP. Overview of Communicable Diseases. Public Health and Preventive Medicine, Wallace BB and Kohatsu N, eds. McGraw Hill, New York, 2007. pp.77-9.

495. Kleiner EA, Wenzel RP. Viral Infections. Public Health and Preventive Medicine, Wallace BB and Kohatsu N, eds. McGraw Hill, New York, 2007. pp.341-52.

496. Van Rijen MML, Bonton M, Wenzel RP, Kluytmans JAJW. Internasal Mupirosin for Reduction of *Staphylococcus aureus* Infections in Surgical Patients with Nasal Carriage: A Systematic Review. *J Antimicrob Chemother* 2008; 61:254-61.

497. Kleiner E, Wenzel RP. Infections in the Compromised Host: Aspergillosis and Candida in Clinical Approach to Infection in the Compromised Host 5th Ed., RH Rubin, LS Young, LR Bada (Eds), 2008 (in press).

498. Powell JP, Wenzel RP. Antibiotic Options for Treating Community-Acquired Methicillin-Resistant *Staphylococcus aureus*. *Expert Review of Antibiotic Therapy* 20087; 6:299-307.

499. Wenzel RP, Bearman G, Edmond MB. Screening for MRSA: A Flawed Infection Control Intervention. *Infect Control Hosp Epidemiol* 2008; 29:1012-8.

500. van Rijen M, Bonton M, Wenzel R, Kluytmans J. Mupirocin ointment for preventing Staphylococcus aureus infections in nasal carriers. Cochrane Database of Systemic Reviews 2006, Issue 4. Art #CD006216.

501. Cecil J, Wenzel RP. Voriconazole. A Review. *Expert Rev Hematol* 2009; 2:237-52.

502. Edmond MB, Wenzel RP. Organizing for Infection Control, in Mandell (ed) Principles and Practices of Infectious Diseases, 2009 (in press).

503. Edmond MB, Wenzel RP. Isolation, in in Mandell (ed) Principles and Practices of Infectious Diseases, 2009 (in press).

504. Wenzel RP, Bearman G, Edmond MB. Further Advances in the Treatment of Methicillin-Resistant *Staphylococcus aureus. European Infect Dis* (in press).

505. Wenzel RP. *ICHE* – 30 years later. *Infect Contr Hosp Epidemio*l. 2010; 31:1-3.

506. Bearman GML, Rosato AE, Assanasen S, Kleiner EA, Elam K, Haner C, Wenzel RP. Nasal carriage of inducible dominant and community-associated methicillin-resistant Staphylococcus aureus in an ambularoty population of predominantly university students. *Internat J Infect Dis*. 2010, Suppl 3:18-24.

507. Wenzel RP, Edmond, MB. Preparing for 2009 HINI Influenza. *N Engl J of Med* 2009; 361:991-3.

508. Wenzel RP. - Minimizing Surgical Site Infections. *N Engl J Med* 2009: 326:75-7 .

509. Wenzel, RP, Genning C, Residual Attributable Mortality: An New Concept for Understanding the Value of Antibiotics in treating Life-Threatening Acute Infections. *ACC* 2010; 54: 4 956-60.

510. Wenzel RP, Infection Control: The Case for Horizontal Rather than Vertical Interventional Programs. *Internat J Infect Dis* 2010; 14 54: 53-5.

511. Methicillin-resistant Staphylococcus aureus: the superbug. Ippolito G, Leone S, Lauria FN, Nicastri E, Wenzel RP *Int J Infect Dis.* 2010 Oct; 14 Suppl 4: S7-11. Epub 2010 Sep 20. Review

512. Wenzel RP. Lessons Learned fromSARS and H1N1 *in* Hospital Infection Control Database for Decision Making – online E-reference R.P. Wenzel and G. Bearman (Eds) – 2012.

513. Wenzel RP. Horizontal versus Vertical Safety Programs in Infection Control *in* Hospital Infection Control Database for Decision Making – online E-reference R.P. Wenzel and G. Bearman (Eds) – 2013.

514. Wenzel RP. Leadership, Management and Politics: Issues for Healthcare Epidemiology *in* Hospital Infection Control Database for Decision Making – online E-reference R.P. Wenzel and G. Bearman (Eds) – 2012.

515. Wenzel RP, Fowler AA, Edmond, MB. Antibiotic Prophylaxis to Prevent Acute Exacerbations of COPD *N Engl J Med* 2012; 367: 340-7.

516. Bearman GM, Rosato A, Elam K, Sanogo K, Stevens MP, Sessler CN Wenzel, RP. A Crossover Trial of Antimicrobial Scrubs to Reduce Methicillin – Resistant Staphylococcus Aureus Burden on Health Care Worker Apparel. *Infec Control Hosp Epidemiol*. 2012 Mar; 33 (3): 268-75. Epub 2012 Jan 6.

517. Wisplinghoff H, Paulus T, Lungenheim M, Stefanik D, Higgins PG, Edmond MB, Wenzel, RP, Seifert H. Nosocomial Bloodstream Infections due to Acinetobacter Baumanii Acinetobacter. Pittii and Acinetobacter Nosocomialis in the United States. *J Infec*. 2012 Mar; 64 (3); 282-90. Epub 2011 Dec 20.

518. Wenzel RP, Edmond MB. Septic Shock – Evaluating Another Failed Treatment. *N Engl J Med* 2012; 366: 2122-4.

519. Vaughan LB, Wenzel RP. Disseminated Toxoplasmosis Preventing as Septic Shock Five Weeks After Renal ransplation Transplant *Infec Dis* 2012, In Press

520. Edmond MB, Wenzel R P. Screening Inpatients for MBSA – Case Closed N *Engl J Med.* 2013 Jun 13; 368(24):2314-5, doi: 10.1056/NEJMe1304831. Epub 2013 May 29.

521. Edmond MB, Wenzel RP Targeted Decolonization to Prevent ICU Infections. N Engl J Med 2013; 369: 1471

522. Wenzel, RP. Acute Tracheitis and Bronchitis. Cecil Textbook of Medicine 2014.

523. Wenzel, RP. Importance of Infection Control in A Guide to Infection in the Hospital Fifth Edition. Ed. G Bearman, M Edmond, M Stevens, RP Wenzel.

524. Wenzel, RP Organization. ibid 2014.

525. Wenzel RP, Antibiotic Resistance ibid 2014.

526. Wenzel, RP, LVAD Infections ibid 2014.

527. Wenzel, RP, Herpes Zoster Infections ibid 2014.

528. Wenzel RP, MERS and the Lessons From SARS ibid 2014.

529. Beydoun K, Forbes B, Wenzel RP. Left Ventricular Assist Device Endocarditis Caused by Vancomycin Intermediate *Staphylococcus Aureus* Successfully Treated with Ceftaroline: A Review of the Clinical Case and Oerview of Vancomycin Resistance in *Staphylococcus Aureus*.
Clin Micro Newsletter. 2013; 35:171-6

530. The Editors of the *N Engl J Med* Contraception at Risk. *N Eng J Med* 2014; 370: 77-8.

531. Wisplinghoff H, Ebbers J, Geurtz L et al Nosocomial Bloodstream Infections due to Candida Spp in the USA: Species distribution, Clinical Features and Antifungal Susceptibilities. *Internal J Antimicrob Agents* 2014; 43: 78-81.

532. Wenzel RP, Edmond, MB. Academic Infectious Diseases in Jeopardy: The Erosion of Time, Professional Values and Physician Satisfaction. *Infection,* 2015, 43: 141-4.

533. Jarrin Tejada C.B., Wenzel RP. Left sided MRSA Endocarditis successfully treated with a combination of Daptomycin and Ceftaroline. Clin Micro Newsletter 2014.

534. Wenzel, RP, Edmond MB. Antibiotics for Abdominal Sepsis. *N Engl J Med* 2015, 372: 2062-3.

535. Ebola. Through Air or Not Through Air: That is the Queston. Ponce de Leon R, Arredondo – Hernandez R, Macias A, Wenzel RP. Front Pub HLTM 2015; 2:292

536. Warner, NC, Vaughan LB, Wenzel, RP. Human Immunodeficiency Virus Associated Thrombotic Thrombocytopenic Purpura, A Clinical Conundrum. J Clin Apher 2016; doi: 10. 1002/jca.21514.

Abstracts/Letters to the Editor

1. Music SI, Wenzel RP, Libonati JP, Snyder MJ, Hornick RB, Woodward TE. Induced human cholera. *J Clin Invest*. 1970;49:69a-70a.

2. McCormick DP, Wenzel RP, Brunner H, Seterfit LB, Beam WE Jr. Reinfection by Mycoplasma pneumoniae. *Abstracts of the Annual Meeting of the American Society of Microbiology.* 1972, p 82.

3. Hendley JO, Sande MA, Wenzel RP, Gwaltney JM Jr. Pneumococcal carriage and acute respiratory disease in families. American Epidemiological Society Meeting, Lexington, Kentucky, April 6-7, 1973.

4. Wenzel RP, Hendley JO, Sande MA, Gwaltney JM Jr. Correlation of serum and nasal influenza antibody. 13th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. September 20, 1973.

5. Wenzel RP, Osterman CA, Gwaltney JM JR. Development of a nosocomial infection surveillance system for hospital infections. Southern Section of the American Federation for Clinical Research, New Orleans, Louisiana, January 1974. Clin Res. 1974;22:38a.

6. Ibid. *Clin Res*. 1974;22:No.3, 456a.

7. Wenzel RP, Hendley JO, Craven RB, Gwaltney JM Jr. Antibody responses to A/30-C707 and A/X-37 influenza vaccines. 1st Intersectional Congress of the International Association of Microbiological Societies, Tokyo, Japan, September 1974.

8. Wenzel RP, Hunting KJ, Osterman CA. Possible airborne transmission of Providencia stuartii within a burn unit. 14th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Francisco, California, September 11, 1974.

9. Craven RB, Wenzel RP, Atuk NO. Control of tuberculosis transmission in the hospital. *Clin Res.* 1975;23:26a.

10. Wenzel RP, Deal EC, Hendley JO. Hospital-acquired respiratory viral infections. *Clin Res* 1975;23:31a.

11. McCarthy MF, Wenzel RP. Nosocomial meningitis in pediatric neurosurgery patients. *Clin Res*. 1975;23:29a.

12. Wenzel RP, Craven RB, Daview JA, Hendley JO, Hamory BH, Gwaltney JM Jr. Field trial of an inactivated *Mycoplasma vaccine. Am J Epidemiol*. 1975.

13. Mandell GL, Rudolph LE, Westervelt FB Jr, Wenzel RP. Prophylactic antibiotic therapy with cefamandole and tobramycin for patients undergoing renal transplantation. International Congress of Chemotherapy, Zurich, Switzerland, April 1977.

14. Veazey JM Jr, Sande MA, Miller LS, Townsend TR, Brokopp CD, Wenzel RP. Transmission of gentamicin-resistant K. pneumoniae and Ps. aeruginosa in a burn unit. 17th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 14, 1977.

15. Wenzel RP, Osterman CA, Townsend TR, Veazey JM Jr, Miller GB Jr, Jackson RS. Statewide surveillance of hospital-acquired infections. 17th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 14, 1977.

16. Tully JG, Rose DL, Whitcomb RF, Wenzel RP. Enhanced isolation of Mycoplasma pneumoniae from human throat specimens with a newly modified culture medium. *Abstracts of the International Organization for Mycoplasmology.* Freidburg, Germany, August 28, 1978.

17. Townsend TR, Wenzel RP. Nosocomial bloodstream infections (BSI) among neonates in a newborn intensive care unit (NICU):a controlled study. 18th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, October 1978.

18. Wenzel RP, Townsend TR, Levine JI, Sande MA. Statewide surveillance for antibiotic audit. *Proceedings of the 1st National Conference on Antibiotic Review*. Atlanta, Georgia, 1979.

19. Wenzel RP, Farber BF. Alternate ways of performing antibiotic review focus on hospital infections: review-based on surveillance data and specific infections. *Proceedings of the 1st National Conference on Antibiotic Review, West Coast Update.* Los Angeles, California, 1980.

20. Wenzel RP. Infection Surveillance systems: choosing an approach for your hospital. *Proceedings of Association for Practitioners in Infection Control*. 1977, 1978.

21. Wenzel RP. Hospital Surveillance of Community infections*. Proceedings of Association for Practitioners in Infection Control.* 1977, 1978.

22. Wenzel RP. Antibiotic audit for small (less than 100-bed) community hospitals. *Proceedings of the 1st National Conference on Antibiotic Review.* Atlanta, Georgia, 1978.

23. Wenzel RP. Working through an antibiotic review for 1-100-bed community hospitals. *Proceedings of the 1st National Conference on Antibiotic Review, West Coast Update*. Los Angeles, California, 1980.

24. Donowitz LG, Wenzel RP. Nosocomial Klebsiella bacteremia in a newborn intensive care unit caused by contaminated breast milk*. Clin Res*. 1979;27:818a.

25. Johns ME, Ryals BM, Guerey TL, Wenzel RP, Rubel EW. Effects of aminoglycoside antibiotics in hair cells of the chick basal papilla. Association for Research in Otolaryngology, St. Petersburg, Florida, January 1980.

26. Townsend TR, Rudolf LE, Westervelt FB, Mandell GL, Wenzel RP. Prophylactic antibiotic therapy with cefamandole and tobramycin for patients undergoing renal transplantation. 18th Interscience Conference on Antimicrobial Agents and Chemotherapy, Atlanta, Georgia, October 1-4, 1978.

27. Wenzel RP. Occurrence, Diagnosis and Source of Hospital-Associated Infections (book review). Handbook on Hospital-Associated Infections. Volume I. WJ Fahlbert and D Gröschel (eds), Marcel Dekker, Inc. New York, New York, 1978. *ASM News*. 1978;44:624-625.

28. Farber BF, Kaiser DL, Wenzel RP. Multivariant analysis of postoperative wound infection rates at 22 community hospitals in Virginia. *Clin Res.* 1980;28:368a.

29. Donowitz LG, Wenzel RP. Nosocomial Klebsiella bacteremia in a newborn intensive care unit caused by contaminated breast milk. 20th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 1980.

30. Farber BF, Kaiser KL , Wenzel RP. Postoperative wound infections: the relationship between infection rate and surgical volume. 20th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 1980.

31. Wenzel RP (Book Review). Hospital-Associated Infections in the General Hospital Population and Specific Measures of Control, Volume 3. D Gröschel (ed), Marcel Dekker, Inc. New York, New York, 1978. *ASM News.* 1980.

32. Martone WJ, Osterman CA, Fisher KA, Wenzel RP. Pseudomonas cepacia: implications of a pseudoepidemic. 20th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 1980.

33. Landry SL, Donowitz LG, Wenzel RP. Hospital-wide surveillance: perspective for the practitioner. *Proceedings of Association for Practitioners in Infection Control.* Atlanta, Georgia, May 1981.

34. Thompson SY, Donowitz LG, Wenzel RP. Infection control policies for surgical procedures performed in outpatient clinics. *Proceedings of Association for Practitioners in Infection Control.* Atlanta, Georgia, May 1981.

35. CDC. Methicillin-resistant *Staphylococcus aureus* in the United States: an endemic hospital pathogen. *MMWR*. 1981;30:557-559.

36. Wenzel RP, Landry SL , Thompson RL. Device-related bloodstream infections with methicillin-resistant *S. aureus*. Bac-Data Perspective on Infection, 1982.

37. Haley CE, Donowitz LG, Thompson SY, Wenzel RP. Emergence of gram-positive bacteria as the major etiology of nosocomial bacteremias in a neonatal intensive care unit. Southern Society for Pediatric Research, New Orleans, Louisiana, January 1982.

38. Thompson RL, Haley CE, Gröschel DHM, Gillenwater JY, Kaiser DL, Wenzel RP. Effect of periodic instillation of hydrogen peroxide into urinary drainage systems in the prevention of catheter-associated bacteriuria (CAB). 22nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Miami Beach, Florida, October 1982.

39. Cabezudo I, Thompson RL, Guenthner SM, Wenzel RP. Efficacy and pharmacokinetics of cefsulodin sodium in cystic fibrosis patients with respiratory infections and Pseudomonas aeruginosa in the sputum. 22nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Miami Beach, Florida, October 1982.

40. Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of bloodstream infections in hospitalized patients. 22nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Miami Beach, Florida, October 1982.

41. Haley CE, Gregory WW, Donowitz LG, Wenzel RP. Neonatal intensive care unit (NICU) bloodstream infections (BSI): emergence of gram-positive bacteria as major pathogens. 22nd Interscience Conference on Antimicrobial Agents and Chemotherapy, Miami Beach, Florida, October 1982.

42. Hoyt JW, Donowitz LG, Wenzel RP. Nosocomial infections in critically ill patients. *Ear Nose Throat J.* 1982.

43. Landry SM, Wenzel RP. Letter to the Editor. *JAMA* . 1983;249:3390.

44. Stillman RI, Donowitz LG, Wenzel RP. The emergence of *Staphylococcus epidermidis* as a hospital wide nosocomial bloodstream pathogen. 23rd Interscience Conference on Antimicrobial agents and Chemotherapy, Las Vegas, Nevada, October 24-26, 1983.

45. Ponce de Leon S, Critchley S, Wenzel RP. A new kind of outbreak: an epidemic of six primary bloodstream infections in a medical ICU caused by nine species. 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Las Vegas, Nevada, October 24-26, 1983.

46. Ponce de Leon S, Guenthner S, Wenzel RP. Microbiologic studies of 50 strains of coagulase-negative staphylococci (CN-S) isolated from the blood of patients with hospital-acquired bacteremia. 23rd Interscience Conference on Antimicrobial Agents and Chemotherapy, Las Vegas, Nevada, October 24-26, 1983.

47. Brawley RL, Wenzel RP. Nosocomial infections: an incidence study of the risk of multiple infections. #516. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

48. Brawley RL, Cabezudo I, Guenthner SH, Hendley JO, Wenzel RP. Evaluation of handwash agents using brief contact time. #520. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

49. Brawley RL, Wenzel RP. Reduction in postoperative wound infection rates: 10-year prospective study of 20,902 operations at the University of Virginia. #524. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

50. Ishak MA, Wade B, Pasquale MA, Gerszten RE, Gröschel DMH, Wenzel RP. Epidemic Legionella micdadei pneumonia in hospitalized patients. #168. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

51. Salata RA, Harmon CP, Scheld WM, Gröschel DHM, Wenzel RP Wade B, Mandell GL. Imipenem/Clastin (I/C) for the treatment of nosocomial pneumonia. #684. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

52. Salata RA, Hayden FG, Rubenstein LJ, Gröschel DHM, Wenzel RP. Acute febrile cerebrovasculitis: clinical and laboratory features. #762. 24th Interscience Conference on Antimicrobial Agents and Chemotherapy, Washington, D.C. October 8-10, 1984.

53. Morrison AJ Jr, Hoffmann KK, Wenzel RP. Pseudomonas maltophilia: spectrum of clinical disease due to an emerging nosocomial pathogen in a university hospital. 25th Interscience Conference on Antimicrobial Agents and Chemotherapy, Minneapolis, Minnesota, September 29 - October 2, 1985.

54. Morrison AJ Jr, Wenzel RP. Nosocomial urinary tract infections due to enterococcus: 10 years experience at a university hospital. 25th Interscience Conference on Antimicrobial Agents and Chemotherapy, Minneapolis, Minnesota, September 29 - October 2, 1985.

55. Morrison AJ Jr, Freer CV, Searcy MA, Landry SM, Wenzel RP. Nosocomial bloodstream infections: secular trends in a statewide surveillance program in Virginia. 25th Interscience Conference on Antimicrobial Agents and Chemotherapy, Minneapolis, Minnesota, September 29 - October 2, 1985.

56. Morrison AJ Jr. Gratz J, Cabezudo I, Wenzel RP. The efficacy of several new handwashing agents in removing non-transient bacterial flora from hands. 25th Interscience Conference on Antimicrobial Agents and Chemotherapy, Minneapolis, Minnesota, September 29 - October 2, 1985.

57. Miller PJ, O Connell JO, Leipold A, Wenzel RP. Potential liability for transfusion-associated AIDS. *International Synopses Periodical.* July 1985.

58. Wenzel RP, Morrison AJ Jr, Stillman R, Landry SM, Ishak MA, Haley R, Freer CV, Norris S, Searcy MA, Ponce de León S. The re-emergence of gram-positive cocci as major nosocomial pathogens. 14th International Congress of Chemotherapy, Kyoto, Japan, June 23-28, 1985.

59. Morrison AJ Jr, Freer CV, Johnston DO, Westervelt F Jr, Normansell DE, Wenzel RP. A seroprevalence survey of HTLV-III antibodies among patients requiring regular dialysis at a university hospital. The National Kidney Foundation, American Society of Nephrology, New Orleans, Louisiana, December 14-16, 1985.

60. Ishak MA, Wenzel RP, Laverdiere M. Pathogenicity and antibiotic resistance among slime-producing strains of coagulase-negative Staphylococci causing nosocomial septicemia. 25th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 29-October 2, 1985. American Society for Microbiology, #656.

61. Miller PJ, O Connell J, Leipold A, Wenzel RP. Letter to Editor, *JAMA*. 1985;255:195-197.

62. Gratz JC, Tartaglino J, Wenzel RP. Comparative in vitro activity of Abbott-56268 (TE-031), a new macrolide against bacteria from nosocomial infections. 26th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 28-October 1, 1986. American Society for Microbiology, #338.

63. Freer CV , Wenzel RP. Mortality, morbidity, and infection intervals in the patient with multiple nosocomial infections. 26th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 28-October 1, 1986. American Society for Microbiology, #510.

64. Morrison AJ Jr, Kaiser DL, Wenzel RP. A measurement of the efficacy of nosocomial infection control using the 95% confidence interval for infection rates. 26th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 28-October 1, 1986. American Society for Microbiology, #1134.

65. Leu HS, Kaiser DL , Wenzel RP. Hospital-acquired pneumonia: attributable mortality and morbidity. 26th Interscience Conference on Antimicrobial Agents and Chemotherapy, New Orleans, Louisiana, September 28-October 1, 1986. American Society for Microbiology, #1149.

66. Wenzel RP, Hayden FG, Gröschel DHM, Salata RA, Young WS, Greenlee JE, Newman S, Miller PJ, Rubinstein LJ, Hechemy KE, Burgdorfer W, Peacock MG. Acute febrile cerebrovasculitis (letter to the editor). *Ann Intern Med*. 1986;105:802-803.

67. Wenzel RP. Overview of epidemiological markers. *Abstracts of 1st International Meeting on Bacterial Epidemiological Markers.* Brussels, Belgium, April 3-4, 1987.

68. Foens C, Wenzel RP. Skin preparation for lumbar puncture (letter to the editor). *JAMA*. 1987.

69. Wey SB, Pfaller MA, Wenzel RP. Attributable mortality and excess length of stay due to nosocomial candidemia. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 4-7, 1987.

70. Martin MA, Perl-DeLisle T, Wenzel RP. Attributable mortality and excess length of stay due to nosocomial coagulase-negative staphylococcal bacteremia. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 4-7, 1987.

71. Pfaller MA, Wey SB, Gerarden T, Houston A, Wenzel RP. In vitro activity of LY121019 versus nosocomial bloodstream isolates of C. albicans. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 4-7, 1987.

72. Helms C, Massanari RM, Wenzel RP, Streed S, Pfaller MA, Moyer N, Hall N, Johnson W, Hausler W Jr. Control of epidemic nosocomial legionellosis: a 5-year progress report on continuous hyperchlorination of a water distribution system. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 4-7, 1987.

73. Hechemy KE, Fox JA, Gröschel DHM, Hayden FG, Wenzel RP. The use of immunoblot to confirm serodiagnostic test results in patients with rickettsial diseases. 27th Interscience Conference on Antimicrobial Agents and Chemotherapy, New York, New York, October 4-7, 1987.

74. Rasley DA, Wenzel RP, Massanari RM, Hierholzer WJ. Organization and activities of the hospital infection control program of the University of Iowa Hospitals and Clinics. *Abstracts of the Annual Infection Control Symposium.* Ulm, Germany, September 22-25, 1987.

75. Pfaller M, Hollis R, Wenzel R. Usefulness of DNA typing in epidemiologic studies of nosocomial candidiasis. 88th Annual Meeting of the American Society for Microbiology, Miami Beach, Florida, May 8-13, 1988.

76. Herwaldt LA, Hollis RJ, Pfaller MA, Wenzel RP. Southern hybridization analysis of plasmid DNA from coagulase-negative staphylococci causing nosocomial bacteremia. 88th Annual Meeting of the American Society for Microbiology, Miami Beach, Florida, May 8-13, 1988.

77. Doebbeling BN, Massanari RM, Pfaller MA, Wenzel RP. Prophylaxis in open-heart surgery: a randomized, controlled comparison of cefazolin and cefuroxime. Interscience Conference on Antimicrobial Agents and Chemotherapy, Los Angeles, California, October 23-26, 1988.

78. Wey SB, Mori M, Pfaller MA, Woolson RF, Wenzel RP. Risk factors for hospital-acquired candidemia: a matched case-control study. 28th Interscience Conference on Antimicrobial Agents and Chemotherapy, Los Angeles, California, October 23-26, 1988.

79. Herdigen R, Hollis R, Houston A, Pfaller M, Wenzel R. Application of three epidemiology typing systems to the study of nosocomial candidemia. 28th Interscience Conference on Antimicrobial Agents and Chemotherapy, Los Angeles, California, October 23-26, 1988.

80. Pfaller M, Barrett M, Koontz F, Rollins N, Wenzel R. Evaluation of a direct fluorescent antibody test for the rapid detection of P. aeruginosa in blood cultures and respiratory specimens. 28th Interscience Conference on Antimicrobial Agents and Chemotherapy, Los Angeles, California, October 23-26, 1988.

81. Pfaller M, Gerarden T, Yu M, Wenzel R. Fungicidal activity of LY121019 alone and in combination with anticapsin and other antifungal agents. 28th Interscience Conference on Antimicrobial Agents and Chemotherapy, Los Angeles, California, October 23-26, 1988.

82. Wenzel RP. Introduction from the Chairman to Symposium on Antiseptics and the Surgical Patient. *J Hosp Infect.* 1988;11(suppl B):3.

83. Wenzel RP. Overview to the Symposium on Antiseptics and the Surgical Patient. *J Hosp Infect* .1988;11(suppl B):51.

84. Perl-Delisle T, Pfaller M, Houston A, Cabezudo I, Wenzel R. Effects of serum on in vitro activity of 11 broad spectrum antibiotics. *Abstracts of 89th Annual Meeting of the American Society for Microbiology.* 1989:30.

85. Doebbeling BN, Wilson ME, O'Deen A, Stagg B, Wenzel RP. Direct costs of universal precautions in a teaching hospital. *Abstracts of 89th Annual Meeting of the American Society for Microbiology*. 1989:49.

86. Pfaller M, Wenzel R, Hollis R, Houston B, Patrick S, Piper J, Win R. Epidemiological typing of Candida parapsilosis. *Abstracts of 89th Annual Meeting of the American Society for Microbiology*. 1989:141.

87. Martin MA, Pfaller MA, Wenzel RP. Coagulase-negative staphylococcal bacteremia. *Ann Intern Med.* 1989;110:946.

88. Martin MA, Pfaller MA, Wenzel RP. *Staphylococcus epidermidis* bacteremia. *Ann Intern Med*. 1989;111:93-94.

89. Martin MA, Pfaller MA, Wenzel RP. Comparative effect of alternative handwashing agents on nosocomial infection rates. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

90. Reagan DR, Pfaller MA, Hollis RJ, Wenzel RP. Molecular epidemiology of nosocomial candidemia. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

91. Cabezudo I, Pfaller MA, Gerarden T, Koontz F, Wenzel RP, Gingrich R, Heckman K, Burns C. Usefulness of the Cand-tec Candida antigen assay in the diagnosis and therapy of systemic candidiasis in high risk patients. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

92. Pfaller MA, Gerarden T, Wenzel RP. Effects of Cilofungin on parameters of cell growth and viability in Candida albicans. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

93. Gorelick K, Jacobs R, Chmel H, Greenman R, the XOMA Sepsis Study Group. Efficacy results of a randomized multicenter trial of E5 anti-endotoxin monoclonal antibody in patients with suspected gram-negative sepsis. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

94. Martin MA, Wenzel RP, Gorelick KJ, The XOMA Sepsis Study Group. Prospective national study of gram-negative bacterial (GNB) sepsis - natural history in the 1980 s. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

95. Bernard GR, Grossman JE, Campbell GD, Gorelick KJ and the XOMA Sepsis Study Group. Multicenter trial of a monoclonal anti-endotoxin antibody (XOMENTM E5) in gram-negative sepsis. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

96. Doebbeling BN, Pfaller MA, Herwaldt LA, Hollis RJ, Wenzel RP. Demonstration of the global distribution of an identical plasmid of *Staphylococcus aureus*. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

97. Veach LA, Pfaller MA, Yu M, Wenzel RP. *Staphylococcus haemolyticus* bacteremia. 29th Interscience Conference on Antimicrobial Agents and Chemotherapy, Houston, Texas, September 1989.

98. Reagan DR, Doebbeling BN, Sheetz CA, Houston AK, Hollis RJ, Pfaller MA, Wenzel RP. Eradication of *S. aureus* nasal carriage: a randomized double blind, placebo-controlled trial. Abstracts of American Society for Microbiology. Anaheim, California, 1990, L. 14:80.

99. Doebbeling BN, Pfaller MA, Bale MJ, Helms CM, Wenzel RP. In-vitro susceptibility of nosocomial gram-negative bloodstream isolates to AT-4140 and other agents. *Abstracts of American Society for Microbiology.* Anaheim, California, 1990, A. 35:40.

100. Wenzel RP, Doebbeling BN, Jones R. Cost benefits of surgical prophylaxis. *Abstracts of International Conference on Prevention of Infection*. Nice, France, 1990.

101. Wenzel RP. The impact of hospital-acquired infections. *Abstracts of International Conference on Prevention of Infection.* Nice, France, 1990.

102. Wenzel RP. Education programs for infection control in the USA. *Abstracts of Hospital Infection Society, International Meeting.* London, England, 1990.

103. Wenzel RP, Stanley G, Pfaller M, Sheetz C, Annis L, Streed S. Clinical trials and handwashing. *Abstracts of Hospital Infection Society, International Meeting*. London, England, 1990.

104. Wenzel RP. Nosocomial bloodstream infections-methodological issues. *Abstracts of Hospital Infection Society, International Meeting*. London, England, 1990.

105. Wenzel RP. The continuing contribution of staphylococci to hospital-acquired infection. *Abstracts of Hospital Infection Society, International Meeting.* London, England, 1990.

106. Wenzel RP, Nettleman MD, Pfaller MA. Can we do more to control methicillin-resistant *Staphylococcus aureus* (MRSA)? *Abstracts of 3rd Decennial International Conference on Nosocomial Infections.* Atlanta, Georgia, 1990.

107. Wenzel RP. Applying epidemiologic techniques to improve quality of care: the role of hospital epidemiology. *Abstracts of 3rd Decennial International Conference on Nosocomial Infections.* Atlanta, Georgia, 1990.

108. Perl TM, Haugen TH, Hollis R, Pfaller MA, Lakeman AD, Whitely RJ, Wenzel RP. Nosocomial transmission of herpes simplex-1 (HSV-1) in an intensive care unit (ICU): a need to reinforce isolation techniques? *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Atlanta, Georgia, 1990.

109. Reagan DR, Huston BM, Hollis RJ, Wenzel RP, Pfaller MA. Evidence of nosocomial spread of *Candida albicans* in a neonatal intensive care unit (NICU). *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Atlanta, Georgia, 1990.

110. Doebbeling BN, Fine BD Jr, Pfaller MA, Sheetz CT, Stokes JB , Wenzel RP. Acute tubular necrosis (ATN) and anion-gap acidosis during therapy with cilofungin (LY-121019) in polyethylene glycol (PEG). *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Atlanta, Georgia, 1990.

111. Doebbeling BN, Omahen J, Lyons J, Wenzel RP. Nosocomial hepatitis A outbreak on a burn unit. *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy*. Atlanta, Georgia, 1990.

112. Doebbeling BN, Hollis RJ, Isenberg HD, Wenzel RP, Pfaller MA. Molecular typing of a *Candida tropicalis* (CT) outbreak in coronary bypass patients. *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Atlanta, Georgia, 1990.

113. Pfaller MA , Wenzel RP. Handwashing: efficacy vs. acceptance. A brief essay. 2nd International Conference of the Hospital Infection Society, London, England, September, 1990.

114. Pfaller MA, Wenzel RP. Feasible and desirable future targets for reducing the costs of hospital infections. 2nd International Conference of the Hospital Infection Society, London, England, September, 1990.

115. Wenzel RP, Pfaller MA. Epidemiology and intervention of hospital-acquired candida bloodstream infection. *Abstracts of 30th Interscience Conference on Antimicrobial Agents and Chemotherapy*. Atlanta, Georgia, 1990.

116. Pittet D, Li N, Omahan J, Tarara D, Wenzel RP. Secondary and polymicorobial bloodstream infections. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy*. Chicago, Illinois, 1991. Abstract #799.

117. Doebbeling BN, Martin MA, Li N, Wenzel RP, and the Xoma Sepsis Study Group. A multivariate model predicting sepsis mortality. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy.* Chicago, Illinois, 1991. Abstract #403.

118. Doebbeling BN, Pfaller MA, Reagan DR, Houston AK, Hollis RJ, Wenzel RP. Investigation of the epidemiology of *Staphylococcus aureus. Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy.* Chicago, Illinois, 1991. Abstract #27.

119. Pittet D, Omahan J, Tarara D, Wenzel RP. Current risk factors for nosocomial bloodstream infection in a tertiary health care center. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy.* Chicago, Illinois, 1991. Abstract #800.

120. Widmer AF, Nettleman MD, Wenzel RP. Clinical impact of culturing central venous catheter tips in a surgical intensive care unit. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy.* Chicago, Illinois, 1991. Abstract #1168.

121. Wenzel RP, Bone R, Fein A, Quenzer R, Schentag J, Gorrlick KJ, Wesel NI, Perl T. Results of a second double-blind, randomized, placebo-controlled trial of anti-endotoxin antibody E5 in gram-negative sepsis. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy.* Chicago, Illinois, 1991. Abstract #1170.

122. Doebbeling BN, Reagan DR, Pfaller MA, Houston AK, Wenzel RP. Long-term follow-up of short-course intranasal mupirocin on the prevalence of *Staphylococcus aureus* nasal and hand carriage. *Abstracts of 31st Interscience Conference on Antimicrobial Agents and Chemotherapy*. Chicago, Illinois, 1991. Abstract #1033.

123. Fisher CJ Jr, Slotman GJ, Opal S, Pribble J, Stiles D, Catalano M, IL-1ra Sepsis Study Group. Interleukin-1 receptor antagonists (IL-1ra) reduces mortality in patients with sepsis syndrome. American College of Chest Physicians Annual Meeting. San Francisco, California, November 7, 1991.

124. Ena J, Houston A, Jones R, Wenzel RP. Trends in gram-positive (GP) bloodstream organism resistance: a seven-year audit of twelve drugs and use data at a large university medical center. General Meeting of the American Society of Microbiology. New Orleans, Louisiana, May 27-30, 1992. Abstract #2844.

126. Perl TM, Lockwood WW, Martin M, Costigan MD, Haynes BS, Wenzel RP. Influence of antiendotoxin antibody (E5) on long-term post-hospital survival after sepsis. *Abstract for American Federation for Clinical Research Meeting.* May 1-4, 1992.

127. Gordon GS, Fisher CJ, Slotman GJ, Opal SM, Pribble JP, Stiles DM, Catalono MA, IL-1ra Sepsis Study Group. Cost-effectiveness of treatment with interleukin-1 receptor antagonist (IL-1ra) in patients with sepsis syndrome. Abstract presented at the Annual Meeting of the American Federation for Clinical Research. May 1-4, 1992.

128. Wenzel RP, Andrivic VT, Bartlett JG, et al. Antiendotoxin monclonal antibodies for gram-negative sepsis (letter). Clinical Infectious Diseases. 1992;14:571-572.

129. Widmer AF, Doebbeling BN, Costigan M, Houston A, Jones M, Wenzel RP. Source of recolonization following elimination of *S. aureus* nasal carriage from chronic carriers. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

130. Pittet D, Wenzel RP. Secular trends in rates and mortality of nosocomial bloodstream infections in a tertiary health care center. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

131. Pittet D, Thievent B, Wenzel RP, Li N, Suter PM. Onset of sepsis APACHE II score is a better predictor of mortality from septicemia than admission APACHE II score in SICU patients. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

132. Pittet D, Wenzel RP. Nosocomial bloodstream infections: secular trends for attributable mortality. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

133. Nafziger DA, Perl TM, Herwaldt LA, Kuhns KR, Hollis RJ, Wenzel RP. Mediastinitis at a tertiary referral hospital. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

134. Widmer AF, Boyken L, Hollis R, Houston A, Wenzel RP, Herwaldt LA. Evaluation of three molecular typing methods of *Staphylococcus aureus (S aureus)* for clinical microbiology laboratories. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

135. Sanford MD, Widmer AF, Bale MJ, Jones RN, Wenzel RP. Evaluation of culture screening methods for detecting patients colonized with methicillin-resistant *S aureus* (MRSA). 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

136. Widmer AF, Li N, Omahen J, Wenzel RP. Challenging an old concept: what is an outbreak? 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

137. Thievent B, Pittet D, Wenzel RP, Li N, Auckenthaler R, Suter PM. Bedside assessment of independent predictors of death from septicemia at three clinically relevant times in SICU patients. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

138. Pittet D, Tarara D, Wenzel RP. Attributable mortality, overall costs, and excess length of stay from nosocomial bloodstream infection in SICU patients. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

139. Pittet D, Thievent B, Wenzel RP, Li N, Suter PM. Active comorbidities determine the prognosis of septicemia in critically ill patients. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

140. Widmer AF, Trilla A, Doebbeling BN, Bale MJ, Wenzel RP, Jones RN. *P aeruginosa* outbreak in a SICU: transmission by hands of a health care worker. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

141. Doebbeling BN, Hollis RJ, Wenzel RP, Pfaller MA, Reagan DR. Prospective evaluation of Candida hand carriage: molecular typing of paired isolates. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

142. Ephtimios IE, Wenzel RP, Doebbeling BN. Fungal bloodstream infections: secular trends at a tertiary care center. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

143. Doebbeling B, Breneman D, Marsh R, Reagan D, Wenzel R. Multi-center study of elimination of *Staphylococcus aureus* nasal carriage with calcium mupirocin ointment in health subjects. 32nd Interscience Conference on Antimicrobial Agents and Chemotherapy. Anaheim, California, October 11-14, 1992.

144. Wherry J, Wenzel R, Wonderink R, Silverman H, Perl T, Nasraway S, Levy H, Bone R, Balk R, Allred R, TNF MAb Study Group. Monoclonal antibody to human tumor necrosis factor (TNF MAb): multi-center efficacy and safety study in patients with the sepsis syndrome. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

145. Voss A, Leick CA, Torremorell Y, Downs DD, Wenzel RP, Doebbeling BN. Handwashing agent use: possible marker for nosocomial infections. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

146. Voss A, Hollis R, Wenzel RP, Doebbeling BN. Investigation of the sequence of colonization and candidemia in nonimmunocompromised patients. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

147. Hollis RJ, Barr J, Wenzel RP. Familial carriage of methicillin-resistant *Staphylococcus aureus* and subsequent infection in a newborn sibling. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

148. Perl TM, Dvorak L, Fu CM, Wenzel RP. Long-term, post-hospital survival after sepsis: influence of antiendotoxin antibody. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

149. Pittet D. Rangel-Frausto S, Tarara D, Costigan M, Wenzel RP. SIRS, sepsis, and severe sepsis: incidence, morbidities, and outcome in SICU patients. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

150. Edmond MB, Hollis RJ, Houston AK, Wenzel RP. Epidemiologic analysis of an outbreak of meningococcal disease. 33rd Interscience Conference on Antimicrobial Agents and Chemotherapy. New Orleans, Louisiana, October 16-20, 1993.

151. Rangel-Frausto MS, Martin MA, Saiman L, Blumberg H, Patterson JE, Pfaller MA, Wenzel RP, the NEMIS Study Group. High prevalence of Candida species on hands of health care workers in surgical and neonatal intensive care units: a multicenter study. *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy*. Orlando, Florida, October 4-7, 1994. #J106, page 105.

152. Edmond MB, Ober JF, Weinbaum DL, Sanford MD, Pfaller MA, Hwang T, Wenzel RP. Risk factors for vancomycin-resistant enterococcal bacteremia. *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Orlando, Florida, October 4-7, 1994. #J157, page 145.

153. Edmond MB, Adams JR Jr, Trilla A, Wenzel RP, Doebbeling BN. Socioeconomic status as a risk factor for nosocomial infection and mortality. *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Orlando, Florida, October 4-7, 1994. #J164, page 185.

154. Rangel-Frausto MS, Pittet D, Costigan M, Tarara D, Happel R, Chiechelly F, Wenzel RP. The epidemiology of the systemic inflamatory response syndrome (SIRS): a prospective study. *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Orlando, Florida, October 4-7, 1994. #J182, page 187.

155. Roy MC, Herwaldt LA, Embry R, Kuhns K, Wenzel RP, Perl TM. Does the NNIS Risk Index (NRI) predict which patients develop wound infection (SWI) after cardiothoracic (CI) surgery? *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Orlando, Florida, October 4-7, 1994. #J209, page 196.

156. Frausto-Rangel MS, Hollis R, Rhomberg P, Sanford L, Pfaller MA, Wenzel RP, Herwaldt LA. Molecular epidemiology of *Legionella pneumophilia* werogroup 1 in a university hospital: a 12-year survey. *Abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy.* Orlando, Florida, October 4-7, 1994. #J233, page 216.

157. Wenzel RP. The economics of nosocomial infections. *Abstracts of the 3rd Hospital Infections Society.* September 4-8, 1994, London, England.

158. Wenzel RP. The role of the hospital epidemiologist in quality assessment. *Abstracts of the 3rd Hospital Infections Society.* September 4-8, 1994, London, England.

159. Wenzel RP. Economic justification of infection control programs. *Abstracts of the 3rd Hospital Infections Society.* September 4-8, 1994, London, England.

160. Perl TM, Frausto-Rangel MS, Wenzel RP, and the TNF alpha MOA Sepsis Study Group. Predictors of mortality in patients with sepsis receiving anti-TNG alpha monoclonal antibody or placebo. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

161. Frausto-Rangel MS, Pittet D, Costigan M, Hwang T, Wenzel RP. Risk factors for septic shock: a matched case control study. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

162. Frausto-Rangel MS, PIttet D, Costigan M, Hwang T, Woolson R, Wenzel RP. The dynamics of disease progression in sepsis: Markov modeling probability for SIRS, sepsis, severe sepsis and septic shock. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20,1995

163. Frausto-Rangel MS, Wiblin RT, Costigan M, Pfaller MA, Wenzel RP and the NEMIS sutdy group. The epidemiology of hospital acquired Candida spp: a mulicenter prospective study. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy*. San Francisco, California, September 18-20, 1995.

164. Wiblin RT, Wenzel RP. Nosocomial enterococcal bacteremia: incidence and mortality. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy*. San Francisco, California, September 18-20, 1995.

165. Berrouane YF, Pfaller MA, Wenzel RP, Herwaldt LA. Epidemiology of fluconazole use at the University of Iowa Hospitals - 1990-1993. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

166. Diekema DF, Messer SA, Hollis RJ, Pfaller MA, Wenzel RP. An outbreak of Candida parapsilosis prosthetic valve endocarditis. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

167. Roy M-C, Herwaldt LA, Wenzel RP, Adams J, Perl TM. Risk factors for surgical site infections (SSI). *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

168. Pfaller M, Messer S, Coffman S, Houston A, Wenzel R, Rinaldi M, and the NEMIS study group. National epidemiology of mycoses survey: a prospective nulticenter sutdy of strain variation and antifungal susceptibility among infecting and colonizing isolates of Candid species. *Abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy.* San Francisco, California, September 18-20, 1995.

169. Wiblin RT, Pfaller MA, Wenzel RP. Nosocomial enterococcal bacteremia: risk factors for mortality. *Abstracts of the 5th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* San Diego, California, April 2-4, 1995. Abstract #18.

170. Frausto-Rangel SM, Pittet D, Hwang T, Woolson RF, Wenzel RP. Transitional probability of SIRS, sepsis, severe sepsis and septic shock. *Abstracts of the 5th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* San Diego, California, April 2-4, 1995. Abstract #M7.

171. Wendt C, Hollis R, Pfaller M, Wenzel R, Herwaldt L. Molecular epidemiology of recurrent gram-negative bacteremia. *Abstracts of the 5th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* San Diego, California, April 2-4, 1995. Abstract #44.

172. Wiblin RT, Wenzel RP. Value of an infectious disease consultantion for nosocomial enterococcal bacteremia. *Abstracts of the 1995 Infectious Diseases Society of America.* San Francisco, California, September 18-20, 1995.

173. Wherry JC, Perl TM, Wenzel RP, and the TNF MAb alpha Norsept I Sepsis Study Group. Characteristics of primary infections and superinfections in sepsis syndrome patients. *Abstracts of the 1995 Infectious Diseases Society of America.* San Francisco, California, September 18-20, 1995.

174. Wenzel RP. Multi-center trial on incidence/risk factors and costs of treating fungal infections. *Abstracts of the 1995 Infectious Diseases Society of America*. San Francisco, California, September 18-20, 1995.

175. Edmond MB, Jones RN, Pfaller MA, Wallalce SE, Wenzel RP. Multicenter surveillance for nosocomial enterococcal bacteremia. A comparison of vancomycin-sensitive versus vancomycin-resistant cases. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #14.

176. Edmond MB, Ober JF, Weinbaum DI, Wenzel RP. National history and attributable morbidity and mortality of vancomycin- resistant enterococcal bacteremia. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #S9.

177. Wiblin RT, Vande Berg J, Costigan M, Huang T, Rangel-Frausto MS, Pittet D, Wenzel RP. Epidemiology of persistent fever and antipyretic therapy in bacteremic septic shock. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #M19.

178. Lundberg J, Costigan M, Bentler S, Dawson J, Nettleman M, Wenzel RP. Staphylococcus aureus bacteremia: The effect of an infectious diseases consultation on patient outcome. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #M89.

179. Lundberg J, Costigan, M, Wiblin RT, Nettleman M, Perl T, Wenzel RP. Septic shock: Analysis of management. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #84.

180. Berrouane YF, Pfaller MA, Wenzel RP, Herwaldt LA. Secular trends of nosocomial deep-seated yeast infections in a university hospital. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America, (SHEA).* Washington, DC, April 21-23, 1996 Abstract #51.

181. Pittet D, Li N, Woolson RF, Wenzel RP. Microbiological factors influencing the outcome of nosocomial bloodstream infections. *Abstracts of the 6th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Washington, DC, April 21-23, 1996 Abstract #79.

182. Pfaller, M.A., Messer, S., Houston, S., Wenzel, W., Rinaldi, M., and The NEMIS Study Group. National Epidemiology of Mycoses Survy: A Prospective Multicenter Study of Strain Variation and Antifungal Susceptibility among Isolates of *Candida* sp. *Abstracts of the 36th Annuanl Interscience Conference of Antimicrobial Agents and Chemotherapy (ICAAC).* New Orleans, LA, September 15-18, 1996.

183. Wilbin, R.T., Vande Berg, J., Lundberg, M., Costigan, M., Rangel-Frausto, M.S., Pittet, D., Wenzel, R.P. Epidemiology of Persistent Fever and Antipyretic Therapy in Bacteremic Septic Shock. *Abstracts of the 36th Annuanl Interscience Conference of Antimicrobial Agents and Chemotherapy (ICAAC).* New Orleans, LA, September 15-18, 1996.

184. Pfaller M., Jones R., Messer S., Houston A., Hollis R., Edmond M., Wenzel R., and The SCOPE Study Group. Strain Variation and Antifungal Susceptibility Among Nosocomial Blood Stream Isolates of *Candida* spp. from U.S. Hosptials Participating in the SCOPE Survey. *Abstracts of the 36th Annuanl Interscience Conference of Antimicrobial Agents and Chemotherapy (ICAAC).* New Orleans, LA, September 15-18, 1996.

185. Wong AHM, Wenzel RP, Edmond MB. Vancomycin-Resistant Enterococcal (VRE) Urinary Tract Infection. *Abstracts of the 7th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* St. Louis, Mo, April 27-29, 1997. Abstract #S3.

186. Bischoff WE, Wenzel RP, Edmond MB. Outbreak of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections Related to Prison Transfers. *Abstracts of the 7th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* St. Louis, Mo, April 27-29, 1997. Abstract #M2.

187. Bischoff WE, Emery CL, Hall GO, Wenzel RP, Edmond MB. Is Liquid Dial ® Soap Effective Against Vancomycin Resistant Enterococci (VRE) and Methicillin Resistant *Staphylococcus aureus* (MRSA)? *Abstracts of the 7th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* St. Louis, Mo, April 27-29, 1997. Abstract #M6.

188. Franchi D, Bischoff WE, Kilpatrick SJ Jr., Wenzel RP, Edmond MB. Dating Multiple Dose Vials (MDV): An Analysis of Location and Content. *Abstracts of the 7th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* St. Louis, Mo, April 27-29, 1997. Abstract #M56.

189. Bischoff WE, Wong MT, Hall GO, Wenzel RP, Edmond MB. Occurrence of Vancomycin-Resistant *Enterococcus faecium* (VREF) Strains in Clinical Isolates. *Program and Abstracts of the Infectious Diseases Society of America(IDSA) 35th Annual Meeting.* September 13-16, 1997. San Francisco, CA. Session 65. Abstract #353.

190. Edmond MB, Jones RN, Pfaller MA, Wallace SE, McClish DK, Campbell L, Wenzel RP. Nosocomial Bloodstream Infections: A One-Year Analysis at 50 US Medical Centers. *Program and Abstracts of the Infectious Diseases Society of America(IDSA) 35th Annual Meeting.* September 13-16, 1997. San Francisco, CA. Session 116. Abstract 660.

191. Bischoff WE, Franchi D, Wenzel RP, Edmond MB. Use of Multidose-Vials in a Tertiary Care Center: Cost Analysis of 30 Day Expiration Policy versus Manufacturer's Expiration Date Policy. *Program and Abstracts of the Infectious Diseases Society of America(IDSA) 35th Annual Meeting.* September 13-16, 1997. San Francisco, CA. Session 118. Abstract 677.

192. Franchi D, Wong AHM, Hall G, Edmond MB, Wenzel RP. Surveillance for Vancomycin-resistant *Staphylococcus aureus* (VRSA) in a High Risk Population. *Program and Abstracts of the Infectious Diseases Society of America(IDSA) 35th AnnualMeeting.* September 13-16, 1997. San Francisco, CA. Session 122. Abstract 741.

193. Bischoff WE, Reynolds TM, Sessler CN, Edmond MB, Wenzel RP. Handwashing Compliance by Health Care Workers: The Impact of an Education and Patient Awareness Program. *Abstracts of the 8th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Orlando, Fl, April 5-7, 1998. Abstract #22.

194. Bischoff WE, Reynolds TM, Hall GO, Wenzel RP. Molecular Epidemiology of Vancomycin-Resistant *Enterococcus faecum* Strains in a Large Urban Hospital over a 5 Year Period. *Abstracts of the 8th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Orlando, Fl, April 5-7, 1998. Abstract #S44.

195. Wong AHM, Abraham DJ, Joshi GS, Wenzel RP. Changes in the Oxyhemoglobin Curve in Sepsis: A pilot study. *Abstracts of the 8th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* Orlando, Fl, April 5-7, 1998. Abstract #S83.

196. Bischoff WE, Reynolds TM, Sessler CN, Edmond MB, Wenzel RP. Handwashing Compliance by Health Care Workers. Impact of an Education and Patient Awareness Program aand the Introduction of a New Hand Disinfectant. *Abstracts of the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy.* September 24-27, 1998. San Diego, CA. Abstract #K-132.

197. Wong MT, Kauffman CA, Standiford HC, Fuchs HJ, Wenzel RP and the Ramoplanin Study Group. Clinical Efficacy and Safety of a Novel Glycopeptide: Ramoplanin, in the Decontamination of the Gastrointestinal System of Patients Colonized with Vancomycin-Resistant Enterococcus. *Abstracts of the IDSA 37th Annual Meeting.* Philadelphia, PA. November 18-21, 1999.

198. King MD, Blumberg HM, Soucie JM, Jarvis WR, Wenzel RP and NEMIS Study Group. Mortality due to Candida Blood Stream Infections (CBSI) in the Surgical Intensive Care Unit (SICU). *Abstracts of the IDSA 37th Annual Meeting.* Philadelphia, PA. November 18-21, 1999. CID publishing number 289.

199. Coudron PE, Tallent SM, Moland ES, Hanson ND, Edmond MB, Wenzel RP. Occurrence of Extended-Spectrum (ESBL) and AmpC Beta-lactamases (BLs) in U.S. Bacteremic Isolates of *Klebsella pneumoniae* (KP): Two Isolates Harbor Inducible Plasmid-Mediated ACT-1-like BLs. 41st ICAAC Abstracts; #C2-2232, p.147, 2001.

200. Borer A, Ostrowsky B, Espinel-Ingroff A, Hall G, Edmond MB, Wenzel RP. In Vitro Activity of Handwashing Agents Against *Candida albicans*. 41st ICAAC Abstracts; #J-116, p.361, 2001.

201. Edmond MB, McClish D, Massi T, Wiblin RT, Kaufman C, Welage L, Goff D, Rex JH, Schuster M, Wenzel RP. Risk Factors for Nosocomial Candidemia Among Patients in Eight Surgical Intensive Care Units. 41st ICAAC Abstracts; #K-1464, p.435, 2001.

202. Borer A, Ostrowsky B, Edmond MB, Bischoff T, McClish D, Wenzel RP. Epidemiology and Risk Factors for Nosocomial *Pseudomonas aeroginosa* Bacteremia in U.S. Hospitals, 1995-2000. 41st ICAAC Abstracts; #K-2043, p.213, 2001.

203. Wenzel RP. Why Does Therapy Fail (Or Appear to Succeed)? 42nd ICAAC Abstracts; #38(L,K)-413, p.450, 2002.

204. Johnson CK, Polk RE, Edmond M, Wenzel RP. Trends in Antimicrobial Use (AU) from 1999 to 2001 in 36 U.S. Hospitals: A SCOPE-MMIT Report. 42nd ICAAC Abstracts; #O-1005, p.419, 2002.

205. Von Baum H, Ober JF, Wenzel RP, Edmond MB. Risk Factors for Nosocomial BSI in a Target Population. 42nd ICAAC Abstracts; #K-88, p.300, 2002.

206. Tallent SM, Christie GE, Edmond MB, Wenzel RP. Characterization of Linezolid Resistance in an *Enterococcus faecium* Isolate from a Nosocomial Bloodstream Infection. *Abstracts of the 9th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).*

207. Marciniak A, Mauskopf J, Wenzel R, Ortiz M, Morris S, Del Favero A, Kibbler C, Rogers T, Schlamm H. Cost-consequence model for comparing voriconazole with conventional amphotericin B as initial antifungal therapy in the treatment of invasive aspergillosis. *Abstracts of the 9th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).* , 2003

208. Herwaldt LA, Cullen J, Hu J, Wenzel RP, Perl TM. Risk Factors for Staphylococcus aureus Nasal Carriage among Surgical Patients. *Abstracts of the 9th Annual Meeting of the Society for Healthcare Epidemiology of America (SHEA).*

209. Marra AR, Barr K, Bearman G, Wenzel RP, Edmond MB. Systemic Inflammatory Response Syndrome in Adult Patients with Nosocomial Bloodstream Infection Due to *Pseudomonas aeruginosa*. *Abstracts of the 15th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America*, April 9-12, 2005.

210. Marra AR, Bearman G, Wenzel RP, Edmond MB. Comparison of Severity of Illness Scoring System for Patients with Nosocomial Bloodstream Infection Due to *Pseudomonas aeruginosa*. *Abstracts of the 15th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America*, April 9-12, 2005.

211. Marra AR, Bearman G, Wenzel RP, Edmond MB. Evaluation of the Charlson Weighted Comorbidity Index and the Maccabe Classification as Predictors of Mortality in Patients with Nosocomial Bloodstream Infection Due to *Pseudomonas aeruginosa*. *Abstracts of the 15th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America*, April 9-12, 2005.

212. Marra AR, Barsanti S, Pires Pereira CA, Gales AC, Rodrigues Cal RG, Menezes LC, Bearman G, Wenzel RP, Edmond MB. Epidemiology and Microbiological Characteristics of Bloodstream Infections (BSI) Due to Metallo-β-Lactamase-Producing *Pseudomonas aeruginosa*. *Abstracts of the 15th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America*, April 9-12, 2005.

213. van Rijen M, Bonten MJM, Pittet D, Weinstein RA, Wenzel RP, Kluytmans JA. Effect of Eradication of *Staphylococcus Aureus* Nasal Carriage Using Mupirocin Nasal Ointment in the Health Care Setting: a Systematic Review. *Abstracts of the 15th Annual Scientific Meeting of the Society for Healthcare Epidemiology of America*, April 9-12, 2005.

Stopped Populating this Field in 2006

RESEARCH SUPPORT SUMMARY

University of Virginia 1972-1986

Sponsor	**# Years of Funding:**	**Project**
National Institutes of Health	1974-78	Study of the Efficacy of an OSU-1 Mycoplasma pneumoniae Vaccine in Marine Corps Recruits
Centers for Disease Control	1974-78	Development of a Statewide Program for Surveillance/Control of Nosocomial Infections
State of Virginia	1978-84	Continuation of CDC Project to Develop Statewide Program for Surveillance and Control of Nosocomial Infections
National Institutes of Health	1985-86	Analysis of Attributable Mortality Data in Nosocomial Pneumonia - Fogerty Award

University of Iowa 1986-1995

Sponsor	**Period**	**Project**	
Cutter Biological	3/87-3/88	Efficacy of Pseudomonas Immune Globulin in the Treatment of P aeruginosa Bacteremia in Compromised Patients	$5,000
Xoma Corporation	3/87-4/89	Efficacy of Anti-Endotoxin Antibody in the Treatment of Suspected Gram-Negative Sepsis	$94,800
Veterans Administration	6/87-2/89	HSR&D/Validation Study of Appropriateness Evaluation Protocol (AEP) Based Method for Estimating Extra Hospital Stay Related to Nosocomial Bloodstream Infections	$ 9,705
Glaxo, Inc.	8/87-8/88	Comparison of Cefzolin to Cefuroxime in Cardiac Surgery	$10,000
Roerig/Pfizer	8/87-12/88	In Vitro Susceptibility of Unique Nosocomial Bloodstream Isolates to new Antibiotics	$18,095
Hoechst-Roussel Pharmaceuticals	1/88-7/88	Effects of Protein Binding on In Vitro Susceptibility of Unique Nosocomial Bloodstream Isolates	$22,000
Lederle Laboratories	8/88-7/89	Comparison of Beta-Lactam Antibiotics Plus Gentamycin-Bloodstream Isolates	$8,500
Calgon Vestal Laboratories	7/87-6/90	Efficacy Study of Handwashing Agents: Calstat vs. Hibiclens	$68,000
ER Squibb and Sons	8/87-7/89	Attributable Mortality of Hospital Acquired Candida septicemia	$20,000

Xoma Corporation	5/89-11/91	Efficacy of Anti-Endotoxin Antibody in the Treatment of Suspected Gram-Negative Sepsis	$157,400
Beecham	6/89-6/90	Efficacy of Mupirocin Ointment for the Eradication of Nasal Mucosa Carriage of Staphylococcus aureus	$53,000
Lilly Laboratories	11/89-11/90	Cilofungin in Disseminated Candidiasis: Dose Ranging Study	$21,605
Fujisawa SmithKline Corporation	1/90-12/90	In Vitro Susceptibility of Unique Nosocomial Bloodstream Isolates to New Antibiotics	$9,750
Hoechst-Roussell	6/90-5/91	Use of Pentoxifylline (Trental) in Patients with Amphetersin B Induced Renal Toxicity - Pilot Study	$11,500
Pfizer	12/90-7/92	Risk Factors Associated with Nosocomial Gram-Negative Bloodstream Infections: A Case Control Study/ Development of a Predictive Mathematical Model for Nosocomial Gram-Negative Bacteremia	$44,825
Pharmaco/ Synergen	4/91-8/92	Human Recombinant Interleukin-1 Receptor Antagonist (IL-Irs) in the Treatement of Sepsis Syndrome	$35,936
Cutter (Miles)	4/91-1/93	Prospective, Double-Blind, Controlled, Randomized, Multi-Center Study of the Safety and Efficacy of TNF MAb for the Treatment of Patients with Sepsis Syndrome	$237,800
Kimberly Clark	8/91-1/92	Sterile Wrap Events Study (Pilot Phase)	$20,460
Pharmaco/ Synergen	7/92-6/93	A Study to Evaluate the Safety and Efficacy of Human Recombination Interleukin-1 Receptor Antagonist (IL-IRA) in the Treatment of Sepsis Syndrome	$41,850
Pfizer Roerig	7/92-6/94	Epidemiology of the SIRS (Sepsis Syndrome)	$352,110
Kimberly Clark	7/92-2/93	Sterile Wrap Study	$62,200
Pact	7/93-6/94	Randomized, Placebo-Controlled Trial of E5 Monoclonal Antibody in Patients with Severe Sepsis	$41,250
Kimberly Clark	8/93-6/94	Sterile Wrap Events Study	$45,000
National	**9/91-8/96**	**Research Training Grant**	**$399,241**

Institutes of Health		**in Hospital Epidemiology (T-32)**	
Merck	12/93-11/95	Multicenter Study to Compare the Safety, Tolerability and Immunogenicity of Three Consistency Lots of VAQTA in Healthy Adults	$47,500
Miles	5/94-2/95	Prospective, Double-Blind, Randomized, Multicenter North American Study of the Safety and Efficacy of TNF MAb for the Treatment of Patients with Septic Shock	$131,885
Hoffman-LaRoche	4/94-6/95	Phase II, Double-Blind, Randomized Placebo-Controlled Study to Evaluate the Safety and Efficacy of 3 Different Doses of Ro 45-2081 in the Treatment of Severe Sepsis/Septic Shock	$47,250
Abbott	9/94-9/95	Achievement Awards Outcomes Research	$50,000
Lederle Laboratories	9/94-9/95	SCOPE: Surveillance and Control Pathogens of Epidemiologic Importance	$208,620
SmithKline-Beecham	9/94-9/95	A Randomized Placebo-Controlled, Double-Blind Comparative Study of Intranasal Mupirocin Ointment for Preventing *S aureus* Surgical Wound Infections	$453,750

1995 - Medical College of Virginia/Virginia Commonwealth University (PI in all but one)

Sponsor	**Period**	**Project**	
Lederle Laboratories	9/95-12/96	SCOPE: Surveillance and Control Pathogens of Epidemiologic Importance	$150,000
Pfizer Inc.	1995- 2001	A Multi-Center Study of the Risk Factors and Outcome of Candida Bloodstream Infections in Surgical ICUs.	$497,284
Rhone-Poulenc	1997- 2001	SCOPE: Surveillance and Control Pathogens of Epidemiologic Importance	$205,000
Pfizer Inc	1997- 2002	SCOPE: Surveillance and Control Pathogens of Epidemiologic Importance	$790,000
Proctor and Gamble	1997- 1998	Handwashing and Predictors of Compliance	$74,000
Rhone-Poulenc	1998	Educational Conference - SCOPE	$250,000
Merck	1999-2002	SCOPE: Pharmacy Component	$300,000
Intrabiotics	1998-2000	Ramoplanin for VRE GI decolonization	$85,000
Pharmacia and Upjohn	2000-2002	Antibiotic resistance in the community	$400,000

Pfizer	2002-2003	SCOPE	$200,000
Cubist	2003	SCOPE	$5,000
Pfizer	2003-2006	SCOPE	$200,000
Pfizer	2006-2007	Epidemiology of CA-MRSA in families (G. Bearman – PI)	$198,000
Gates Foundation	2007-2008	Educational award to invite 74 women from developing Countries to attend the International Society for Infectious Diseases Congress in Kuala-Lampur – June 2008 (RP Wenzel – PI)	$250,000
VCU Partnership Award	2009 -2012	Educational Grant to Develop Lectures and International Visitors – VCU International Program in Infecton Control	$ 25,000

Dr. Richard Wenzel
Exhibit B

Plaintiffs' Expert Report of Michael W. Buck

Plaintiffs' Expert Report of Said Elghobashi

Plaintiffs' Expert Report of William Jarvis

Plaintiffs' Expert Report of Dr. Jonathan M. Samet

Defendants' Expert Report of Theodore R. Holford, PhD

Defendants's Expert Report of Dr. Jonathan Borak, MD, DABT

Deposition Transcript and Exhibits of Mark Albrecht

Deposition Transcript and Exhibits of Scott Augustine, MD

Deposition Transcript and Exhibits of Robert Gauthier, MD

Deposition Transcript and Exhibits of Andrea Kurz, MD

Deposition Transcript and Exhibits of Paul McGovern, MD

Deposition Transcript and Exhibits of Michael Reed, MD

Deposition Transcript and Exhibits of Daniel Sessler, MD

Allegranzi B, et al. New WHO recommendations on intraoperative and postoperative measures for surgical site infection prevention: an evidence-based global perspective. *The Lancet Infectious Diseases* 16.12 (2016): e288-e303.

Berríos-Torres SI, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. *JAMA surgery* (2017).

Birgand G, et al. Air contamination for predicting wound contamination in clean surgery: A large multicenter study. *American Journal of Infection Control* 43.5 (2015): 516-521.

Bohl MA, et al. The Barrow Randomized Operating Room Traffic (BRITE) Trial: An Observational Study on the Effect of Operating Room Traffic on Infection Rates. *Neurosurgery* 63 (2016): 91-95.

Graves N, et al. A cost-effectiveness modelling study of strategies to reduce risk of infection following primary hip replacement based on a systematic review. *Health Technology Assessment (Winchester, England)* 20.54 (2016): 1.

Hewitt DB, et al. Reducing colorectal surgical site infections: a novel, resident-driven, quality initiative. *The American Journal of Surgery* 213.1 (2017): 36-42.

Hickson CJ, et al. Prophylactic antibiotics in elective hip and knee arthroplasty. *Bone and Joint Research* 4.11 (2015): 181-189.

Jensen CD, et al. Return to theatre following total hip and knee replacement, before and after the introduction of rivaroxaban. *Bone & Joint Journal* 93.1 (2011): 91-95.

Jonsson EO, et al. Bacterial contamination of the wound during primary total hip and knee replacement: median 13 years of follow-up of 90 replacements. *Acta orthopaedica* 85.2 (2014): 159-164.

Le Manach Y, et al. Outcomes after hip fracture surgery compared with elective total hip replacement. *Jama* 314.11 (2015): 1159-1166.

McGovern PD, et al. Forced-air warming and ultra-clean ventilation do not mix. *J Bone Joint Surg Br.* 2011; 93-B:1537-44.

Mora M, et al. Microorganisms in confined habitats: Microbial monitoring and control of intensive care units, operating rooms, cleanrooms and the International Space Station. *Frontiers in Microbiology* 7 (2016).

Nickinson RSJ, et al. The microbiology of the infected knee arthroplasty. *International Orthopaedics* 34.4 (2010): 505-510

Rafiq I, et al. The microbiology of infected hip arthroplasty." *International Orthopaedics* 30.6 (2006): 532-535.

Sprowson A, et al. Changing antibiotic prophylaxis for primary joint arthroplasty affects postoperative complication rates and bacterial spectrum. *The Surgeon* 11.1 (2013): 20-24.

Stocks GW, et al. Directed air flow to reduce airborne particulate and bacterial contamination in the surgical field during total hip arthroplasty. *The Journal of Arthroplasty* 26.5 (2011): 771-776.

Tai V, et al. Results of observational studies: analysis of findings from the Nurses' Health Study. *PloS one* 9.10 (2014): e110403.

Tayton ER, et al. The impact of patient and surgical factors on the rate of infection after primary total knee arthroplasty. *Bone Joint J* 98.3 (2016): 334-340.

Tsai J, et al. Forced air warming device failure resulting in smoke and soot on a surgical patient. 2016. Poster Presentation.

Walcott BP, et al. Infection following operations on the central nervous system: deconstructing the myth of the sterile field. *Neurosurgical Focus* 33.5 (2012): E8.

Weinstein RA and Marc JMB. Laminar airflow and surgical site infections: the evidence is blowing in the wind. *The Lancet Infectious Diseases* 17.5 (2017): 472-473.

Weiser MC and Calin SM. The current state of screening and decolonization for the prevention of Staphylococcus aureus surgical site infection after total hip and knee arthroplasty. *J Bone Joint Surg Am* 97.17 (2015): 1449-1458.

Supplemental Report Prepared for Blackwell Burke

In re Bair Hugger Forced Air Warming Devices Products Liability Litigation

On 30 August 2017, William Maisel, MD, MPH, Deputy Center Director for Science, Center for Devices and Radiological Health, U.S. Food and Drug Administration, sent a notice to health care providers (attached) titled: "Information about the Use of Forced Air Thermal Regulating Systems – Letter to Health Care Providers." In the notice, the FDA concludes "[t]herefore the FDA continues to recommend the use of thermoregulating devices (including forced air thermal regulating systems) for surgical procedures when clinically warranted."

Based on my review of the FDA notice, the FDA notice is in keeping with my June 2, 2017 report and expert opinions. I include the FDA notice as part of the materials considered for my expert opinions and on which I rely for my expert opinions. If asked at the time of trial, I will include the August 30, 2017 FDA notice as evidence supporting my expert opinions.

I certify, under penalty of perjury, that my statements in this supplemental report, dated September 7, 2017, are true and correct.

Richard P. Wenzel, MD, MSc

Dated 7 September, 2017

Information about the Use of Forced Air Thermal Regulating Systems- Letter to Health Care Providers

August 30, 2017

Dear Health Care Provider,

The FDA is reminding health care providers that using thermoregulation devices during surgery, including forced air thermoregulating systems, have been demonstrated to result *in* less bleeding, faster recovery times, and decreased risk of infection for patients.

The FDA recently became aware that some health care providers and patients may be avoiding the use of forced air thermal regulating systems during surgical procedures due to concerns of a potential increased risk of surgical site infection (e.g., following joint replacement surgery). After a thorough review of available data, the FDA has been unable to identify a consistently reported association between the use of forced air thermal regulating systems and surgical site infection.

Therefore, the FDA continues to recommend the use of thermoregulating devices (including forced air thermal regulating systems) for surgical procedures when clinically warranted. Surgical procedures performed without the use of a thermoregulation system may cause adverse health consequences for patients during the postoperative and recovery process.

Forced air thermalregulating systems, also called forced air warmers or forced air warming systems, are devices used to regulate a patient's temperature during surgical procedures. Forced air thermal regulating systems use an electrical blower to circulate filtered, temperature controlled air through a hose into a blanket placed over or under a patient.

To determine if there is an increased risk of surgical site infection when forced air thermal regulating systems are used during surgery, the FDA collected and analyzed data available to date from several sources, including medical device reports received by the agency, information from manufacturers and hospitals, publically available medical literature, operating room guidelines, and ventilation requirements

As always, please follow the manufacturer's instructions for use in the operating room/and or the post-operative environment.

FDA ACTIONS

The FDA will continue to actively monitor this situation and will update this communication if significant new information becomes available.

CONTACT US

If you have questions about this communication, please contact CDRH's Division of Industry Communication and Education (DICE) at DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV), 800-638-2041 (tel:800-638-2041), or 301-796-7100 (tel:301-796-7100).

Sincerely,
/s/
William Maisel, MD, MPH
Deputy Center Director for Science
Center for Devices and Radiological Health
U.S. Food and Drug Administration

More in Letters to Health Care Providers (/MedicalDevices/Safety/LetterstoHealthCareProviders/default.htm)

EXHIBIT DX2

TO DECLARATION OF MARY S. YOUNG IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE OPINIONS AND TESTIMONY OF RICHARD WENZEL, M.D.

UNITED STATES DISTRICT COURT

DISTRICT OF MINNESOTA

- -

In Re:

Bair Hugger Forced Air Warming

Products Liability Litigation

This Document Relates To:

All Actions MDL No. 15-2666 (JNE/FLM)

- -

DEPOSITION OF RICHARD P. WENZEL, M.D., MSc.

VOLUME I, PAGES 1 - 370

AUGUST 4, 2017

(The following is the deposition of RICHARD P. WENZEL, M.D., MSc., taken pursuant to Notice of Taking Deposition, via videotape, at the Hausfeld law firm, 1700 K Street Northwest, Suite 650, in the City of Washington, District of Columbia, commencing at approximately 9:08 o'clock a.m., August 4, 2017.)

APPEARANCES:
On Behalf of the Plaintiffs:
Gabriel Assaad
KENNEDY HODGES
4409 Montrose Boulevard
Suite 200
Houston, Texas 77006
Ben Gordon
LEVIN PAPANTONIO, P.A.
316 S. Baylen Street
Suite 600
Pensacola, Florida 32502
Genevieve M. Zimmerman
MESHBESHER & SPENCE, LTD.
1616 Park Avenue
Minneapolis, Minnesota 55404

On Behalf of the Defendants:

Corey L. Gordon
Peter J. Goss
BLACKWELL BURKE P.A.
431 South Seventh Street
Suite 2500
Minneapolis, Minnesota 55415

ALSO PRESENT:
Ronald M. Huber, Videographer

EXAMINATION INDEX

EXHIBIT INDEX

P R O C E E D I N G S

(Witness sworn.)

RICHARD P. WENZEL, M.D., MSc.,
Called as a witness, being first
duly sworn, was examined and
testified as follows:

EXAMINATION

BY MR. ASSAAD:

Q. Please state your name.
A. Richard Wenzel.
Q. And what's your current address?
A. 1420 Mosquito Point Road, White Stone, Virginia. Home address you wanted.
Q. Yeah. And your business address, if you have one?
A. The post office is P.O. Box 901, and again White Stone, Virginia, 22578, so.
Q. Are you still affiliated with Virginia Commonwealth University?
A. Yep. I'm still teaching. I'm sort of formally retired, but they bring us back every now and then. So I -- I teach.
Q. Have you had your deposition taken before?
A. Never.
Q. This is your first time?

A. Yeah.
Q. Is this your first time being an expert witness in a case?
A. No. I've been asked questions four other times. Want to hear about those, or?
Q. Four other times?
A. Yeah.
Q. I'll get to that in a second.
Since this is your first deposition I'm going to go through the rules very carefully.
A. Sure.
Q. I'm going to ask you numerous questions. If you don't understand the question, please let me know. Fair?
A. Yes.
Q. If you answer the question, I'll assume that you understood the question. Fair?
A. Yes.
Q. At any time you want to take a break, please let me know. I just ask that you request a break after you answer a pending question. Fair?
A. Yes.
Q. And if at any time you want to correct an answer later on that you gave previously, just please let me know, we can always go back.

A. Good.
Q. Today I am representing over 2700 plaintiffs in a multidistrict litigation, and my goal is to understand all your opinions today and to understand what you are going to be testifying at trial.
Do you understand that?
A. Yes, I do.
Q. So I want a clean record, and I don't want any -- if there's anything that needs to be corrected, it's better to correct it today because I will not have another opportunity -- or I may not have another opportunity to take your deposition again.
Do you understand that?
A. I do.
Q. Okay. And also, for the court reporter, please wait till I finish my question before you begin answering even though you might know what the question is, and I'll also wait for your answer before I ask my next question so that we have a clean record and we don't upset the wonderful court reporter that's taking down all our words.
Do you understand that?
A. Yes.
Q. Now you've been asked to be an expert in this case; correct?

A. That's right.
Q. Okay. And you understand as an expert you are to be objective; correct?
A. Yes.
Q. Not an advocate for either side. You understand that.
A. I'm not an advocate.
Q. Okay. How is it that you became involved in this case?
A. Guessing roughly two and a half years ago a representative from Greenberg Traurig called me.
Q. And who was that?
A. And it was Evan Holder.
Q. Evan Holden?
A. "Holder." "Holder," I think it is.
Q. It's Holden.
A. Is it? Sorry about that. Been awhile.
Q. And that was for the Walton case?
A. Yes, it was.
Q. And do you know how --
Were you referred to them by someone, or?
A. He told me that he had spoken to Michelle Stevens and Michelle Stevens said I was an infectious disease person and he asked me if I'd look at the records.

Q. Do you know Michelle Stevens?
A. I do.
Q. How do you know Michelle Stevens?
A. Roughly starting in 2009. As background, I had been invited to Mexico during the height of the H1N1 epidemic in April of 2009. It was a fascinating experience that you don't want to hear about right now, but about that time I recognized that the high-risk patients, this is before anybody knew anything, were obese patients and pregnant patients, and they were all about 21 years old. I made rounds in ICUs.
I was asked by, I'm trying to think of her name, Deborah Gardner from -- who's an administrator with 3M, if I'd be willing to go to four countries in South America as part of their infection control education program. And I think that that first trip I think also involved Mexico. So that was later on in 2009, and I was very excited because I got a chance to go back to Mexico to get a follow-up of what I had observed, and also now it was the winter in South America so they were undergoing their own beginning epidemic --
Q. I don't mean to interrupt. I don't need that much detail. I just want to know --

A. Okay.
Q. -- how and when you met her.
A. Okay. So that -- So basically on that trip, she came on the trip and she was a pediatric infectious disease, I was an adult infectious disease. Basically I wound up giving about three lectures per city in each country --
Q. So you met her on the trip?
A. -- and visited a lot of hospitals there.
Q. Okay. You met her on the trip.
A. Yeah.
Q. Okay. In Mexico. Fair enough.
Have you --
Do you consult for 3M?
A. One time I did.
Q. At what time? At what period of time?
A. Probably three, four years ago they asked me one question, if I would review a meta-analysis related to one of the drapes that they had. So unrelated to the Bair Hugger.
Q. Okay. And were you paid for that?
A. I was.
Q. And how much -- how much per hour were you paid for that?
A. Six hundred dollars an hour, and best that I

can remember it was about 10 hours.
Q. Do you still keep in touch with Michelle Hulse Stevens?
A. No, haven't.
Q. You were issued a subpoena in this case. Do you recall that?
A. I do.
Q. Okay. And you reviewed the subpoena?
A. I did.
Q. Okay. And the subpoena requested that you produce documents by June 21st, 2017. Do you recall that?
A. I do.
Q. Did you produce all your documents that were responsive to the subpoena to counsel?
A. Yeah. I actually pulled everything, sent it over to counsel and they sent it on.
Q. Okay. What's been placed in front of you is a pile of documents that was produced to the plaintiffs today in response to your subpoena that were supposedly due to the plaintiffs on June 21st, 2017.
Are those the documents that you produced to defense counsel in this case responsive to the subpoena?

A. I think --
MR. COREY GORDON: I move --
THE WITNESS: Wait. Okay.
MR. COREY GORDON: -- to strike counsel's characterization and want to note for the record that we interposed an objection to certain of the subpoena requests. In the ensuing time period we have re -- revisited those objections, and even though we believe that what -- that the stack of materials is -- would be protected, we have decided to waive that and go ahead and make that available to you, which we did today. So there -- You can now ask your question.
BY MR. ASSAAD:
Q. Did you produce those documents to your counsel by June 21st, 2017?
A. Yeah. I made the deadline.
Q. And would you agree with me that the stack is about a foot high?
A. It's a foot high, yeah.
Q. Okay. And that contains all of the articles that you reviewed?
A. I don't know if it's all of them, but all the ones I underlined for sure.
Q. Okay. So many of those documents have

underlines in them?
A. Yeah. I'm kind of a nerd and underline a lot of stuff, yeah.
Q. Okay. And many of those documents --
MR. BEN GORDON: That was produced, too. That's also his.
Q. Oh I forgot, we have another -- we have another thing to add to the pile so now it's over one foot. You agree?
A. Yes, I do.
Q. Okay. And so those documents are documents that you have highlights on, or underlines?
A. Yes.
Q. Documents that you have notes on?
A. Yes.
Q. You actually have actually handwritten notes on regular paper as well?
A. I think I do. I don't --
Q. If you look at --
There's a yellow sheet there and a couple other sheets.
A. Yeah.
Q. Okay. You have -- You have deposition transcripts?
A. I think I re --

Yeah. The ones that I looked at, yes.
Q. And you spent a lot of time on this case; correct?
A. I did.
Q. Okay. Do you think it's fair that I get a foot and a half set of documents on the day of your deposition to review when I only have seven hours to take your deposition?
MR. COREY GORDON: I object to the question, lack of foundation. Also calls for a legal conclusion.
As I noted, we interposed an objection. That's not Dr. Wenzel's decision. We also made the decision, the lawyers, to produce these in spite of what we believe to be a valid objection.
MR. ASSAAD: Objection noted.
Q. Do you think it's fair, as a layman, that you, who spent over 300 hours on your report and reviewed all these documents, that I get a foot and a half or a foot and a quarter of documents on the day of your deposition?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
Q. You may answer.
A. So my view was to get the documents to the

law offices, and after that it's their decision.
Q. I mean, do you think it'd be fair if I gave you a foot and a half of documents on the day of the deposition and expect you to answer questions on it?
MR. COREY GORDON: Same objections.
Q. "Yes" or "no"? Do you think it's fair?
A. Well --
MR. COREY GORDON: Same objections.
MR. ASSAAD: It's a simple question. It's a simple question.
MR. COREY GORDON: Wait, wait.
MR. ASSAAD: I got your objection. You said "same objection." No speaking objections.
Q. You may answer the question.
MR. COREY GORDON: Gabe -- Gabe, let me stop you right now. If we're going to have another episode like we did last week --
MR. ASSAAD: You call the judge. You can call the judge. You produced a foot and a half of documents on the day of deposition. I am happy with that. You want to do that?
(Interruption by the reporter.)
MR. ASSAAD: I'm just asking if it's -- if he would think it would be fair if I gave him a foot and a half of documents on the day of deposition.

MR. COREY GORDON: As a courtesy to the court reporter, if no one else, I am simply asking you, Mr. Assaad, to try to chill out a little bit and wait until either Dr. Wenzel has finished his answer, I have finished my objection before you launch into whatever you want to -- want to speak about.
MR. ASSAAD: I will give you a continuing objection that my line of questioning is objectionable.
MR. COREY GORDON: No. I'm not going to take a continuing objection. I will interpose objections --
MR. ASSAAD: Okay.
MR. COREY GORDON: -- as I see fit. I just ask you to give me and the witness and the court reporter --
MR. ASSAAD: I --
MR. COREY GORDON: -- the courtesy of not talking -- trying to talk over us. We -- We went through an unpleasant --
MR. ASSAAD: I got -- I got -- I got it, Corey.
MR. COREY GORDON: You're doing it right now, Gabe.
MR. ASSAAD: Well Corey, you don't need to

waste time. We don't have a lot of time, we have a huge expert report to go through that he spent 300 hours on.
Q. I'm just asking if he thinks it would be fair if I gave him a foot and a half of documents on the day of his deposition to answer questions on.
MR. COREY GORDON: My objections are the same.
A. Again, what I would say is I met my obligation to get the documents to the legal firm on time.
Q. So you don't want to answer my question, is that --
A. No, I mean, I think it would be -- if you gave me this to read in one day, yeah, that would be challenging.
Q. Okay. It would be challenging; correct?
A. Yes.
Q. Okay. I mean, from --
I mean, you wouldn't expect to give one of your students a foot and a half of documents and to answer questions on it in seven -- in seven hours; would you?
A. No, probably not.
Q. Okay. Are all the documents that you

produced to counsel listed in your expert report?
A. I think so.
Q. Okay. You do understand that today you're under oath; correct?
A. I do.
Q. And that's under penalty of perjury; correct?
A. That's correct.
Q. If you realize that anything in your report is incorrect or wrong, this is the time to inform us. Do you understand that?
A. I do.
Q. Okay. Now it's my understanding, from reading your report, that you don't believe that infections can be caused by airborne contaminants in the operating room. Is that true?
A. I don't think that's exactly what I said. I think the key element of my report is I couldn't find evidence linking the Bair Hugger to harm, and then I went through a great deal of papers to show that I think most infections, the vast majority, come from the patient's own microbiome. I'm not sure that's your question, but that...
Q. So you -- it's your opinion that most of the infections that occur during a total knee or total hip

arthroplasty come from the patient's own biome, microbiome.
A. Yes, I do.
Q. Okay. And that's based on research that you reviewed?
A. Research that I reviewed, yeah.
Q. Okay. And we'll get to that soon.
And when we're talking about infections during total hip/total knee arthroplasty we're talking about any type of infection, not infections that may be caused by a Bair Hugger, correct, that are caused by the human biome?
A. I'm not sure. The question again?
Q. Well before you limited to your -- your opinion that the Bair Hugger doesn't cause infections. Do you recall that?
A. Yeah. What I said is I couldn't find evidence that would link the Bair Hugger to any link to infections.
Q. Okay. My question is: With respect to just total hip and total knee, irrespective of the source of the -- or what may or may not cause the infections, it's your opinion that the majority of those infections are caused by bacteria on the patient's own biome.

A. I do, yes.
Q. Okay. Is it my understanding that the majority of the time you spent on formulating your opinions was doing a literature review?
A. Yes.
Q. Okay. You didn't do any biological testing; correct?
A. That's correct.
Q. You looked at no internal 3M documents; correct?
A. That's correct.
Q. Okay. You didn't do any particle testing; correct?
A. That's correct.
Q. Okay. In fact you haven't -- you didn't do any type of original testing.
A. Not related to this case.
Q. Okay. Your report is largely a recitation and cri -- of critiques of various peer-reviewed studies; correct?
A. It's my review of the peer-reviewed studies, and my conclusions based on the data that I saw and my interpretation of the data.
(Wenzel Exhibit 1 marked for identification.)

BY MR. ASSAAD:
Q. What's been marked as Exhibit 1 is a copy of your report. Do you agree with me that that is a complete copy of your report?
A. It looks like it.
Q. Okay. And have you had a chance to review your report before today's deposition?
A. Yes, I have.
Q. Okay. You've reread your entire report before today's deposition?
A. I have.
Q. Okay. And you --
Is there anything that you want to change in your report before we begin?
A. I don't think so, but we'll see.
Q. Sitting today, these are your complete opinions and all of the sources that you rely upon to formulate your opinions as of June 2nd, 2017 when you submitted this report.
A. Are there other articles out there, are you asking, --
Q. No.
A. -- that I might have thought about since then, or?
Q. Well I'm asking about articles and

literature that you rely upon.
A. Yeah.
Q. And that you've cited and have reviewed to support your opinions in your report. They're all contained in this report of Exhibit 1; correct?
A. Either here or the materials that I sent to you, yeah.
Q. Okay.
MR. COREY GORDON: And I want -- so you can ask him about it, I want you to know we are going to ask him to offer an opinion of the valid -- the validity of the recently published Scott Augustine thing.
MR. ASSAAD: I understand that, but I think before I'm going to ask him any questions on that he should file a supplemental report so I can prepare, and to prepare what his opinions are going to be and we can come back and take his deposition.
MR. COREY GORDON: So will you agree to that with your experts as well, who've rendered -- who've supplemented their opinions based on the newly published Augustine whatever it is?
MR. ASSAAD: We'll you've already asked them questions on it, but I will consider it.
BY MR. ASSAAD:

Q. Now let's turn to page 73 of your report. You noted on the bottom of page 73, on the third paragraph from the bottom, "Dr. Jarvis' deposition is superficial and wanting."
Do you see that?
A. I do.
Q. Okay. What deposition did you read by June 2nd, 2017?
A. I -- I read his deposition. Is that what you're asking me?
Q. You signed this on June 2nd, 2017; correct? Next page, sir.
A. Yeah. No, I see that.
Q. Okay. What deposition did you have of Dr. Jarvis that you want to criticize him as being superficial and wanting?
A. Yeah, I don't know why the days don't match.
Q. Well did you not check your report to see if it was accurate?
A. I did.
Q. Okay. Do you agree with me that this is not accurate?
A. Well I agree that I have the 2nd written down there, and I don't know why -- I did read Dr. Jarvis's deposition, and I thought it was at the time

that I did this report.
Q. Well, sir, for the -- his deposition was after June 2nd, 2017.
A. When was his deposition?
MS. ZIMMERMAN: Last Tuesday.
Q. Last Tuesday.
A. Oh, that's probably his report, then, that I'm talking about, if that's true.
Q. So you're saying this is not accurate.
A. I'm saying that I should have had the word "report" there.
Q. Instead of "deposition"?
A. Instead of "deposition."
Q. Okay. So you agree that's a mistaken your report.
A. I agree and apologize.
Q. Okay. And so you want to criticize Dr. Jarvis to say that his -- that his opinions are superficial and wanting before you even had a chance to read his deposition?
A. I saw it based on his report.
Q. Okay. Page 74, third paragraph. You indicate that "Dr. Samet's deposition is uncritical and wanting." It seems like you like the word "wanting"; correct?

A. I did say the word "wanting" and again --
Q. What does "wanting" mean to you?
MR. COREY GORDON: Gabe, let him finish his answer. You're going to -- You're starting it again.
A. Well again, I thought it was very uncritical. You want me to tell you why about both of these people?
Q. No. So you thought it was uncritical and wanting, but you didn't have a chance to read his deposition by that date; correct?
A. No. This -- I should have said --
Q. Okay.
A. -- his report. A mistake.
Q. Okay. Another mistake; correct?
A. Yes.
Q. Okay. So now you agree that there are mistakes in your report.
A. In terms of those words, yes.
Q. Okay. And there may be some others that we'll point out later on.
A. Don't know.
MR. COREY GORDON: Object to the form of the question, move to strike.
Q. Now do you agree that all the articles that you cited are authoritative?

MR. COREY GORDON: Object to the form of the question.
Q. In your report of Exhibit 1?
A. If I cited them they gave some insight, I think, in ter --
Q. So you'd rely --
A. Huh?
Q. So you'd rely on -- on the articles that you cited.
MR. COREY GORDON: Object to --
A. Some much more than others.
THE WITNESS: I'm sorry.
MR. COREY GORDON: Object to the form of the question.
MR. ASSAAD: Basis?
MR. COREY GORDON: "Reliance" is a legal term, and if you want to ask him what he, as a scientist, was doing, that's fine. But you're -- you're -- you're trying to, you know, as you just did, try to --
MR. ASSAAD: I got your objection.
MR. COREY GORDON: -- impose a legal term.
MR. ASSAAD: I got your objection.
Q. Do you know what the term "rely" means?
A. In legal terms, no.

Q. How about in scientific terms?
A. Yeah. Scientific terms I would say, yeah, it's credible evidence.
Q. Okay. And do you know what "authoritative" means?
A. Usually by someone who's thought to be reputable.
Q. Okay. And you understand when I refer -- if I ask you if an article is authoritative?
A. Yeah. You might want to -- I would probably want to add some weight to that or not, some more weighty than others in terms of the force of the data available.
Q. It's my understanding that you have cited, I mean, last time I counted, between -- in your -- in your report, like, over 90 articles in your -- in your expert report; correct?
MR. COREY GORDON: Objection, --
A. I don't know.
MR. COREY GORDON: -- lack of foundation.
A. I don't know how many there were. There were a lot.
Q. You've read your report; correct?
A. I have.
Q. And there are many -- you cite to many

different articles; correct?
A. I do.
Q. And it's my understanding that you read those articles completely; correct?
A. If I cited it, I read those articles.
Q. You didn't just read the abstract.
A. I did not read just the abstract.
Q. Okay.
(Wenzel Exhibit 2 marked for identification.)
BY MR. ASSAAD:
Q. What's been marked as Exhibit 2 is a list of articles that -- and documents that you considered or reviewed; is that correct?
A. That's correct.
Q. But they may not be cited in your report; correct?
A. I think that's true.
Q. Okay. Do you consider all of the articles in Exhibit 2 to be authoritative?
MR. COREY GORDON: Object to the form of the question.
A. I don't know if they're authoritative. They're -- They're articles I read related to the case.

Q. Did you rely on them in formulating your opinions?
A. Some of them I didn't actually use in my report.
Q. That wasn't my question, sir.
Did you rely -- Did you rely on them in formulating your opinions, whether or not you cited them in your report?
MR. COREY GORDON: Same objections.
A. Yeah, for the most part I think that's true.
Q. The answer to my question is "yes."
A. Yes.
Q. Okay. Going to Exhibit B, it seems like you received the report of -- the expert report of Michael Buck. Do you see that?
A. Where is that?
Q. First line.
A. Yeah.
Q. But you offer no criticisms in your report of Michael Buck; correct?
A. No. I didn't spend much time on that, no.
Q. So the answer to my question is you didn't offer any criticisms of Michael Buck in your report; correct?
A. I did not. That's correct.

Q. Okay. You also looked at the report of Dr. Said Elghobashi; correct?
A. Yes.
Q. In your report you didn't offer any criticisms of Dr. Elghobashi in your report; correct?
A. That's true.
Q. Did you even understand his report?
A. It was way over my head.
Q. Okay. I understand that you criticize Dr. Jarvis as being -- I'd like to use the words you used -- "superficial and wanting"; correct?
A. That's correct.
Q. Okay. And you also criticized Dr. Jonathan Samet in your report as being "wanting" as well; correct?
A. That's correct.
Q. Did you have any criticism of Dr. Holford's report?
A. No.
Q. Why not?
MR. COREY GORDON: Object to the form of the question.
A. I thought he was helpful, actually.
Q. Have you read his --
(Interruption by the reporter.)

Q. Did you rely on his opinions in formulating your opinions?
A. In -- In part, where he talked about the changing rates, for example, over time during the Bair Hugger period, when he showed the high rates at that hospital compared to the rest of the U.K. hospitals in the same trust. There were a couple of things like that that made me even more skeptical of the articles that were focusing on --
Q. You're talking about the McGovern article.
A. McGovern article.
Q. So would you agree -- would you defer to Dr. Holford with respect to his analysis of the McGovern article?
MR. COREY GORDON: Object to the form of the question.
A. No, I don't think I would defer to him at all. I think I have my own opinion.
Q. Okay. But you relied on some of the information you obtained from his report in formulating your opinions.
A. A little bit of that, yes.
Q. Okay. With respect to Dr. Borak, do you have any criticism of his report?
A. No. I thought he did a good job.

Q. Okay. Did you rely on any information in Dr. Borak to formulate your opinions?
A. Yes. I -- In his report -- I want to make sure I don't mix up his report with his deposition. I think -- Yeah. His -- His focus on the rivaroxaban issue, I -- I thought was very helpful, added to what I thought was going on.
Q. Okay. So did you rely on information in his report to formulate your opinions, some of your opinions?
A. Perhaps.
Q. Is that a "yes" or a "no"?
A. Yeah, I think it's a yes, but I -- you know, I can't exactly remember what parts.
Q. You don't consider yourself an expert in hypothermia; do you?
MR. COREY GORDON: Object to the form of the question.
A. No, in the sense that where hypothermia inter -- interfaces with infectious disease I think I know a lot, yes.
Q. What research have you done with hypothermia?
A. I've done no direct research with it.
Q. So you're just basically relying on

literature review to -- for your understanding of hypothermia as related to surgical-site infections.
A. Well with the background in infectious diseases and interest in hospital-acquired infections. If that's part of the mix, yes.
Q. Well you graduated from medical school in 1965; correct?
A. That's correct.
Q. And a lot of the research regarding the effects of hypothermia on -- and its effect on surgical-site infections was much after 1965. Do you agree?
A. No question. Yes.
Q. Okay. So a lot of the --
I mean, you have done no research on that issue independently; correct?
A. That's correct.
Q. Okay. And you've done no studies on that; correct?
A. No studies.
Q. Okay. So you agree that most of the information that you've obtained was through peer-reviewed articles that other people have done in the area; correct?
A. That's correct.

Q. Okay. And you'd agree with me that the two leading people dealing with the effects of hypothermia in the world are Dr. Andrea Kurz and Dr. Daniel Sessler; correct?
A. Yes.
Q. Okay. So you would defer to them with respect to the effects of hypothermia on surgical-site infections; correct?
A. I don't know --
MR. COREY GORDON: Object to the form of the question.
A. -- if I'd defer to them, no.
Q. So you wouldn't defer to a doctor that has spent their entire life doing research on an issue, that -- that has published tens of articles on that issue, has given talks around the world on that issue, and continues to do research on that issue, you wouldn't defer to them on issues of hypothermia?
MR. COREY GORDON: Object to the form of the question.
A. What I would do is look at what they have written and see if that comports with all the other data that are out there, and look at their articles themselves so I would formulate an opinion. I'm not intimidated by the whole raft of research that someone

else has done to say I'm not going to have a thought on it.
Q. So you wouldn't defer to Dr. Sessler or Dr. Kurz with respect to hypothermia and surgical-site infections.
A. Not necessarily. I'd like to know exactly what you're getting at so I can comment on it.
Q. Well who else out there has done research with respect to hypothermia and the incident of surgical-site infections?
A. Well I looked at two clinical trials, I cited those both in my report. And Melling was the second one after Kurz. I cited Madrid's recent meta-analysis. There's also an earlier meta-analysis, I cited the author, and -- and that came in a publication in AORN, Eileen Scott's. I cited six cohort studies of people who've done work in hypothermia. I cited a case-control study about hypothermia and infections. I cited eight studies looking for anything that the Bair Hugger may have done in terms of colony-forming units, which would be maybe a step in the pathway of infections.
Q. Sir, I'm not -- I'm not talking about Bair Hugger. I'm talking about hypothermia and the incidence of SSI.

A. Yeah. And I've cited the -- well SSI -- Yeah.
So I think I've given you a -- a number of papers to look at that.
Q. Okay. You've never spoken on the issue of hypothermia and effects of surgical-site infections; correct?
A. I've spoken on surgical-site infections where I've cited work on hypothermia, but I haven't just given a talk just hypothermia.
Q. Okay. Have you read the deposition of Dr. Sessler?
A. Yeah. I don't remember that very well, but yeah.
Q. Do you remember the deposition of Andrea Kurz?
A. I do.
Q. Okay. And you read that one?
A. Yes.
Q. Okay.
MR. ASSAAD: Mark this as Exhibit 3.
(Wenzel Exhibit 3 marked for identification.)
MR. ASSAAD: I don't have a copy for you.
MR. COREY GORDON: That's fine. Just note

that that came out of the box of materials.
MR. ASSAAD: I was about to say that.
MR. COREY GORDON: That's fine.
BY MR. ASSAAD:
Q. Exhibit 3 came out of the documents that were produced today; correct, doctor?
A. I think that's right, yes.
Q. Okay. Where'd you obtain that document from?
A. This one I think I got from counsel, but I'm not sure.
Q. So is that the only document of Exhibit 3 that you obtained from counsel?
A. No.
Q. What other document --
A. Are there other documents, you mean, that they may have sent to me to read?
Q. Yes.
A. Is that what you're asking?
Q. Well Is that -- Let me rephrase.
Is that the only internal document, like non-peer-reviewed literature that you received from counsel?
MR. COREY GORDON: Object to the form of the question.

A. Not sure, but probably.
Q. Okay. So you didn't receive any internal testing of the Bair Hugger from 3M?
A. No.
Q. You didn't receive any --
Did you receive any of the computational fluid dynamics studies that were done internally by 3M?
A. No.
Q. Did you receive any of the schlieren studies that were done internally by 3M?
A. No.
Q. Did you see --
Did you get any of the calculations done with respect to whether or not the Bair Hugger disrupts unidirectional flow that was done internally by 3M?
A. No.
MR. COREY GORDON: Object to the form of the question.
MR. ASSAAD: Basis?
MR. COREY GORDON: Assumes facts not in evidence, and -- and the predicate of the question is actually contrary to evidence.
MR. ASSAAD: Okay.

Q. Did you receive any of the -- Strike that.
Did you see the computational fluid dynamic videos perfor -- prepared by Dr. Elghobashi?
A. Was that a Science Day? I can't remember --
Q. No.
A. -- whether he had one. Then I probably didn't see it.
Q. Did you see the videos prepared by Dr. Abraham?
A. I think he had that at Science Day. That's all I saw, yes.
Q. Okay. But my understanding is because your opinion is that most of the infections that cau -- most of the bacteria that causes surgical-site infections is on the patient's flora, that airflow in the operating room is -- is not that -- is not as important as other areas with respect to infection.
MR. COREY GORDON: Object to the form of the question.
A. What I would say is that if you're looking for the reservoir of the organisms causing surgical-site infections, my opinion is that they come from the patient the vast majority of time.
Q. When you say "vast majority," can you give me a percentage?

A. Well in my report I've said somewhere between 70 and 90 just based on the data that we have already.
Q. Okay. And that is because, based on your opinion that if a surgical-site infection occurs that it's -- it's most likely patient flora and not from airborne contamination.
MR. COREY GORDON: Object to the form of the question.
A. It's based on my opinion, which is based on review of the literature that looks at the microbiome and the influence of the microbiome on the organisms causing surgical-site infections.
Is that clear, or let me know if you --
Q. Well no. I'm just trying to understand your opinion --
A. Yeah.
Q. -- and just to sum it up.
A. Sure.
Q. Your opinion is that the most likely cause of a surgical-site infection is the pla -- the patient's flora.
A. Yes.
Q. Okay. And you don't believe that the -- that the air quality of an operating room causes a

significant risk of surgical-site infection.
MR. COREY GORDON: Object to the form of the question.
A. Well I'm not sure what you mean by "significant risk," but I think -- I mean, I belie -- I'm interested in infection control, no question, and I would love the air to be as clean as possible. And the question really gets to the heart of this is does air influence the infections or the infection rate, and it's hard to find a lot of data to support that.
Q. Well --
A. I -- I don't want to say it's a total impossibility. I'm one of those guys, you'll ask me a lot of questions, I won't say "never" or "always."
Q. Well let's do it this way to make things easier. I'm asking for your opinion within a reasonable degree of medical probability. Okay?
A. Umm-hmm.
Q. I'm not asking for a hundred percent certainty.
A. Yeah.
Q. You understand that?
A. Yeah.
Q. So it's my understanding that your opinion is that the mo -- that -- that more likely than not

the air quality in an operating room does not cause a significant risk in surgical-site infections.
MR. COREY GORDON: Object to the form of the question.
A. I don't know that I would phrase it that way.
What I would say is most -- the origin, in other words, the reservoir of the organisms causing surgical-site infections is the vast majority are going to be in the patient, they're endogenous, in my opinion. I -- You know, I want the air to be as pure as possible. I think there's always a possibility that air is involved in surgical-site infections. I think the information that we'd love to have to answer your question is -- is still not out there clear. And the reason, in part, if you want to look at laminar airflow. So right after the Lidwell's really interesting study, you know, heart and lung, number of patients, 8,000 patients, randomized, you know, a lot of hospitals began to then rely on laminar airflow. So what happened then? So you had Brandt's study, you know, the total review, and then you had Gastmeier's review, and then you had a review by Hooper for the New Zealand and the follow-up New Zealand; four cohort studies, 300,000 patients, and what they found

actually was the infection rates were a little higher if you had laminar airflow.

Follow that up. More recently Bischoff has done a big meta-analysis published in Lancet, and what he showed was in fact with 14 studies, hips and knees, there is no real improvement when you add all those data as well from the meta --

Q. Can I ask you a question real quick?

A. Hmm?

Q. Can I ask you a question real quick?

A. Yeah.

Q. What percentage of hospitals in the United States use laminar airflow?

A. I don't know what the answer is. I don't think it's the majority.

Q. I mean, have you ever been in an operating room in the United States that has laminar airflow?

A. Don't think so.

Q. Do you know what laminar airflow is?

A. Unidirectional filtered air.

Q. That's your understanding of laminar airflow?

A. Yeah. I'm not an expert in laminar.

Q. Okay. So when you read studies that discuss laminar airflow and turbulent airflow, --

A. Yeah.

Q. -- do you -- don't you think it's important to understand the difference?

A. Yeah.

Q. Okay.

A. I think I do.

Q. So what --

So your difference is one is unidirectional, and the --

And what's "turbulent" then?

A. Turbulent is where there's no effort to sort of compartmentalize the air either from the side or from the top that laminar flow is trying to push down the particles or -- in one way or another.

Q. So what's turbulent, then? Where is the air coming from?

A. Turbulent they don't have that. The air is ambient air coming through a filter that's in the operating room.

Q. But where are the -- where is -- where is the vents?

MR. COREY GORDON: Objection, lack of foundation.

A. I don't know.

Q. I mean, doctor, you agree with me that if

you're going to criticize articles and use it to formulate your opinions that you should have -- especially discussing laminar flow and turbulent flow, you should have a good understanding of what the difference is. Don't you agree?

MR. COREY GORDON: Object to the form of the question.

Q. Don't you agree, doctor?

A. I'd love to know more about laminar flow, but I've -- I've cited 300,000-plus patients who undergo laminar flow, and then I've cited a meta-analysis recently.

Q. But would it make any difference if 99 percent of the hospitals in the United States don't use laminar flow?

MR. COREY GORDON: Object to the form of the question.

A. I don't even understand that question.

Q. Well you --

Do you know what percentage of hospitals in the United States use laminar flow?

A. No, I don't. I thought it was a minority.

Q. Do you think if air comes from the ceiling that it's laminar flow?

MR. COREY GORDON: Object to the form --

A. No, not necessarily.

MR. COREY GORDON: -- of the question, lack of foundation.

Q. Okay. So why would you compare laminar flow to turbulent flow in a case in the United States of America where most of the patients are in turbulent airflow operating rooms in your report, if it's completely irrelevant?

MR. COREY GORDON: Object to the form of the question.

A. No. You asked -- You asked me a question about the importance of air, and then I went back to say -- and you said, is it not important or important, something along that line. Then I went back to talk about Lidwell's study that stimulated the really international push for laminar flow, and --

Q. I understand the studies.

MR. ASSAAD: I'm not asking for him to describe the studies, Corey. We're going to have a long day, we're going to --

MR. COREY GORDON: No. Let's make short-circuit. Are you prepared to stipulate that studies on laminar airflow are irrelevant to this case?

MR. ASSAAD: No. No. But when it comes to

infection -- I'm just ask -- I'm trying to see if understands what laminar flow is.
MR. COREY GORDON: Okay. Well you've asked him that.
MR. ASSAAD: Well he's --
BY MR. ASSAAD:
Q. You're criticizing laminar flow as compared to turbulent flow.
A. Yeah.
Q. You do understand we're in the United States of America and this case is here; correct?
A. Pardon me?
Q. The case is here in the United States of America.
A. Yes, they are.
Q. Okay.
A. Yeah.
Q. And if you're looking at infection rates with respect to what happens in the United States, if the majority of the United States operating rooms do not -- do not contain laminar flow, then the issue between laminar and turbulent is irrelevant; correct?
A. Well --
MR. COREY GORDON: Object to the form of the question, also lack of foundation.

A. You know, I'm trying to respond to the question of how important air is, and --
Q. I'm talking about laminar and turbulent, sir, --
A. No, I understa --
Q. -- I'm not talking about --
A. No. I understand.
So what I'm saying is if you want to look at the difference, laminar flow clearly has been shown to decrease particles. And the question is does decreased particles really relate to the endpoint surgical-site infections. So I've cited data from four large cohorts, over 300,000 patients, and then an additional 14 patients in a meta-analysis by Bischoff, and an accompanying editorial by Weinstein that talks about you don't need laminar flow. So that's -- that's a lot of data.
Q. Do you know what the velocity of air is in a laminar flow system in Australia?
A. I don't know what the velocity is in Australia.
Q. In the United Kingdom?
A. No.
Q. Do you know what it is in New Zealand?
A. No.

Q. Okay. Don't you think the velocity of air has a lot to do with how air flows in an operating room?
A. May well, --
MR. COREY GORDON: Object to the form of the question.
A. -- but I don't know.
Q. You would defer to an engineer; correct?
A. About velocity, yes.
Q. About airflow in an operating room; --
A. Yes.
Q. -- correct?
A. Yes.
Q. You'd defer to a -- someone that's a -- that's an expert in fluid dynamics; correct?
MR. COREY GORDON: Object to the form of the question.
A. Fluid dynamics to talk about air, you mean?
Q. Yes.
A. Yeah, I'll talk about the clinical studies, and they can talk about the basic science of airflow, absolutely.
Q. Are you familiar with Memarzadeh?
A. With what?
Q. Memarzadeh?

MR. COREY GORDON: Object to the form of the question.
Q. Do you know who he is?
A. I don't think so.
Q. Okay.
MR. ASSAAD: What was the basis?
MR. COREY GORDON: Memarzadeh? I mean, if you want to ask him about a specific study or -- I mean, there are proba --
MR. ASSAAD: Who he is. Who he is.
MR. COREY GORDON: You know, Gabe, I'll bet --
Q. Do you know who Darouiche is? Do you know who Darouiche is?
MR. COREY GORDON: I'll bet there's several hundred people in the United States whose last name is Memarzadeh.
MR. ASSAAD: Okay Corey, great.
Q. Do you know who Darouiche is?
A. I do.
Q. How many Darouiches are there in the United States, do you think?
A. I have no idea.
Q. Okay. But you know the Darouiche I'd be talking about in this case; correct?

A. Yes.
Q. Okay. You mentioned particles in an earlier answer. Do you agree that particles can carry bacteria?
A. Yes, some of them can.
Q. What do you mean by "some of them"?
A. I think the -- I've seen sort of percentages vary, plus or minus 40 percent or something like that.
Q. What percentages carry parti --
In an operating room, what percentage of the particles carry bacteria?
MR. COREY GORDON: Object to the form of the question.
A. Well I don't know, but I'm giving you what I've seen printed in the literature, 40 percent.
Q. Forty percent of the particles in an operating room carry bacteria?
MR. COREY GORDON: Object to the form of the question.
A. Forty percent of particles can carry bacteria. I don't know how well that's been studied in an operating room by itself, but I'm happy to talk about particles.
Q. Well, so -- Do you have a --
Do you have a citation for that?

A. No, I don't.
Q. Okay.
(Wenzel Exhibit 4 marked for identification.)
BY MR. ASSAAD:
Q. Exhibit 4 is a copy of your curriculum vitae. Is this the most up to date copy of your curriculum vitae?
A. I think so.
Q. Are you board certified in infectious disease?
A. I'm board certified in infectious disease and internal medicine.
Q. Okay. I don't want to spend too much time, but please help me out here. I want to go to your publications --
A. Sure.
Q. -- which I believe starts on page -- under your Bibliography. There's no page numbers. I'm sorry.
A. Yeah, there should be. I'm sorry.
Q. Well that's what was provided to me.
Is that another mistake?
A. Well --
MR. COREY GORDON: Object to the form of

the question.
A. -- I don't know if it's a mistake. I wish they were there to help you.
Q. Okay. The bibliography sometimes your name is first and sometimes it's last or in the middle. What does that mean with respect to published papers?
A. If you're the first author it's you're the one who really did the work, you were at the front line doing the work and should get the credit as the first author. If you're the last author you're usually the person -- the senior member of the team, helped design the study and helped perhaps with the protocol.
Q. Okay. And you have text books, and journal/book section editor, books for general readership, and monographs. What are the difference between them?
A. Okay. So under the papers, these are -- tend to be peer-reviewed articles published in journals.
Q. Umm-hmm.
A. Monographs are sometimes just someone might say, would you give us a review of something like surgical-site infections, for example, and you put together a brief sort of report that's not peer

reviewed. It might be for a meeting, for example.
If you're asking me about the --
What's the other thing you asked about, I guess books or something like that --
Q. Yeah.
A. -- I wrote? Yeah, I've written -- published already one novel and one non-fiction book, and that's totally separate from the science side.
Q. I think I said "textbooks." I think you have eight textbooks here.
A. Oh, I'm sorry. Textbooks. What are textbooks?
Q. No. I mean, what's the difference between a textbook and a monograph?
A. Oh a monograph is usually a very brief sort of summary on a particular topic.
Q. Can a monograph be authoritative?
A. Less steps than a textbook. Textbooks should be highly referenced in general, so.
Q. So the "Handbook on Hospital Acquired Infections," you're the author of that; correct?
A. That's correct.
Q. Published in 1981; correct?
A. Yes.
Q. You could --

A. What pa -- Well let me just -- I'll go try to find.
Q. It's under "BIBLIOGRAPHY."
A. Yeah. Yeah, go ahead.
Q. Are you there?
A. Yeah. Thanks.
Q. Do you consider that book authoritative?
A. Yes.
Q. Okay. Do you consider all your writings authoritative?
A. Well I'm biased, but of course I think I do.
Q. Okay. Were you --
Did you write that whole book or were you just the editor?
A. No, I'm the editor. When you see all of these basically I'm the editor, and may have written one or more chapters.
Q. But as the editor you -- you review everything in the book?
A. Yeah, unfortunately.
Q. And you agree with everything that's in the -- in the -- in --
A. I don't know if I'd agree with everything, but at the time that the articles came across I thought they were reasonable.

Q. What do you mean by "reasonable"?
A. That they summed up the literature accurately. If you ask me to go back, for example, to a 1981 publication, do I still believe that? I may not agree with that.
Q. Science advances over time; correct?
A. No, I'm with you.
Q. Otherwise we'd be stuck in the stone age; correct?
A. I'm with you.
Q. Okay. And -- And even though something might be appropriate at the time, some sort of procedure or medication, later on you might find out that it's -- could be harmful to the patient; correct?
A. Sometimes that happens, yes.
Q. Okay. I mean, it happens with many products in the world. I mean, we have recalls; correct?
MR. COREY GORDON: Object to the form of the question.
A. Yeah, we do have recalls, meaning -- that's where I guess the government, you mean, gets involved, or the FDA.
Q. Or it could be a voluntary recall; correct?
A. Yes, it could be. That's right.
Q. I mean, you expect corporations to be

responsible and not put out harmful products into -- into the market; correct?
A. Well I'm an infection control person. I don't want any harmful products.
Q. Okay. And in fact, you know, you are an infectious disease person and you would understand that a joint infection is a very serious infection.
A. I've seen a number of patients with prosthetic joint infections. Taking care of them, it's a big deal; they suffer physically, emotionally, sometimes financially. They often have miserable follow-up with repeated INDs, incision drainage. They often have a spacer put in, so then -- then they have the prosthesis taken out and put in. So I feel very sorry for those patients, no question.
Q. And some of them die.
A. Occasionally die.
Q. I mean, it's not like an infection, you know, like strep or something that my kid gets.
A. Strep can kill you, by the way. I don't want to trivialize --
Q. I understand that.
A. -- you or your child.
Q. But, I mean, much more money is spent on, you know, fixing a joint infection than -- than strep

in the United States.
A. Joint infections are somewhere between 50 and $90,000 a case is what it's been estimated at. Strep throat, a lot less.
Q. I mean, you agree with me that a joint infection is probably one of the worst infections a person can get in their lifetime.
A. Well there are a lot of bad things you can get out there, but it's on my list, and I would pre -- you know, I would put it on your list as a -- if I were consulting with you. I'd say, you don't want this one either. You don't want Ebola, you know, you don't want Zika, you don't want the horrible flesh-eating strep, and you don't want a hip infection after a prosthetic joint.
Q. And therefore you would agree that doing everything possible to eliminate joint infections should be done.
MR. COREY GORDON: Object to the form of the question.
A. I'm an infection control person. I would love to minimize the risk as much as possible.
Q. For example, if you found out that there was a device in the operating room that was contaminating the sterile field, you wouldn't want that device in

the operating room unless it was absolutely necessary; correct?
A. Well you're going to get to the Bair Hugger I'm sure with that question, but, I mean, I would want as few organisms around as possible, but I would say as an epidemiologist does that itself link directly to infections, and so I would want to know that.
Q. Well safety is paramount; correct?
MR. COREY GORDON: Object to the form of the question.
A. Safety -- Safety is very important paramount, sure.
Q. I'm not talking about the Bair Hugger, I'm just talking about in general. I mean I hope, as a doctor, if you find out that the device is unsafe and causes harm to a patient, you wouldn't use it; correct?
A. Given those statistics I would not want to use it.
Q. Okay. And you would agree with me as a doctor that's maybe performing total hip or total knee arthroplasties, that you want to do everything you can to prevent a joint infection because you know how severe a joint infection is.
MR. COREY GORDON: Object to the form of

the question, lacks foundation, as -- assumes facts not in evidence.
A. So when you say everything that -- I mean I try to prepare the patients before surgery, that kind of thing?
Q. You want to do everything from -- from -- from cleanliness of the operating room, to patient prep, to procedure, technique, to limit the -- the risk of surgical-site infection during a total hip and total knee because of the devastating nature of those types of infections.
A. They're definitely devastating, and I would want the systems in the hospital and the personnel in the hospital and the environment to be as clean as possible. I want to lower the rates as much as they can be lowered.
Q. I mean, you wouldn't advise keeping a device or instrument in the OR that is contaminated and can increase the risk of a surgical-site infection.
MR. COREY GORDON: Object to the form of the question.
A. So, you know, there's nothing sterile, or not much sterile in an operating room. The table itself isn't sterile that you put a patient on. So if you talk about contamination, do I want to go in and

try to irradiate the table, as an example. I'd say, you know, that may be overkill. That table has never been linked to an infection. You know, recently there's some studies that looked at using bioluminescence, for example, and the -- this -- the tray that you put the instruments on, that's not totally sterile. It should be. But if that's not linked to an infection would I want to get rid of the tray, is that what you're saying?
Q. Then you need to really listen to my question, sir.
A. Okay. I'll try to.
Q. Let me read my --
A. Yeah.
Q. I said -- I said contaminated and increases the risk of infection.
A. If you say both, yes.
Q. Okay. That's exactly what I said.
A. Okay. I was -- I didn't --
Q. Let me read the question again.
A. Yeah. Go ahead. I didn't hear that first I guess.
Q. You wouldn't advise keeping a device or instrument in the OR that is contaminated and can increase the risk of surgical-site infection.

Do you agree with that?
MR. COREY GORDON: I object to the form of the question.
A. And shown to increase.
Q. Yes.
A. Not a rare potential, one in a million, but shown in the -- in the literature to increase infections. If you say it that way, yes.
Q. Okay. In the literature?
A. If somebody's done a study, in other words.
Q. Okay.
A. That's what I'm trying to say. Documentation. So you say it's contaminated and linked to infections, I would say, how is it linked to infection, hopefully in some study.
Q. But does it have to be in the literature, or can it be just from scientific evidence or common sense?
A. Common sense, no. There's a lot of people -- You know, there's a guy by the name of Galileo who defied common sense and found out that, you know, the earth's not the center of the universe. It was common sense before that.
Q. Okay. Do you agree it's the responsibility of the corporation that manufactures a medical device

to make sure it's safe?
MR. COREY GORDON: Object to the form of the question.
A. Manufacturers do what?
Q. A medical device to make sure it's safe?
A. I think, yeah, again, I'm interested in infection control, I'm interested in safety. If somebody makes a device, I would hope that they would make it safe.
Q. And they're the -- they're responsible for making sure it's safe. Don't you agree?
A. I would hope --
MR. COREY GORDON: Same objection.
A. -- so, yeah.
Q. And in fact, I mean, you've been part of studies, haven't you, where corporations fund studies of their own products to determine whether or not it's clinically effective and safe?
A. I've done a number of studies on drugs, for example, used to treat sepsis, and to a one they were all failures.
(Interruption by the reporter.)
(Discussion off the stenographic record.)
A. To a single one. To every one of them. I'm

sorry. To a case, if you will, they were all failures.
Q. And --
A. And we published, by the way.
Q. I understand that.
And those studies were funded by the manufacturer of those drugs; correct?
A. By the pharmaceutical company, yeah.
Q. Okay. Because no one else is going to fund a study regarding their own product.
A. Yeah. It's hard sometimes to get NIH to fund private industry.
Q. Okay. So usually private industry usually funds their own studies to determine the safety of their -- of their product; correct?
MR. COREY GORDON: Object to the form of the question.
A. Well certainly for drugs, which I have a lot of experience with, I -- you know, I haven't really -- I don't think I have any studies that I've done on products.
Q. Okay.
A. Well urinary catheter apparatus, I have done studies on those.
Q. And who funded that study?

A. Hmm?
Q. Who funded that study?
A. It was funded by the industry itself, yeah.
Q. Okay. Because industry wants to --
A. They --
Q. -- perform studies to not --
A. Show the safety of their product.
Q. You have to let me finish.
A. I'm sorry. I'm sorry.
Q. The manufacturer wants to fund studies to -- to determine whether or not it's effect -- like clinically effective or a good product, and to determine whether or not it's safe; correct?
A. Yes, that's true.
Q. Because safety is paramount; correct?
MR. COREY GORDON: Object to the form of the question.
MR. ASSAAD: Basis?
A. Safety is a --
MR. COREY GORDON: "Paramount" is a -- is -- presumes everything. Safety is an important consideration, but you can -- you can have a perfectly safe operation that guarantees that there's no surgical-site infections by not doing the surgery.
MR. ASSAAD: I'm asking --

MR. COREY GORDON: There's a balance.
MR. ASSAAD: I'm asking for the legal basis, not your --
MR. COREY GORDON: The legal balance is that the word "paramount" is vague.
MR. ASSAAD: Okay. Then say "vague."
MR. COREY GORDON: You were using it in a particular context and he --
MR. ASSAAD: For the rec --
MR. COREY GORDON: -- he may interpret it and -- as may the jury, in a different context.
MR. ASSAAD: For the record, I asked for the objection to my question, and Corey Gordon could have said just, "vague"; however, he went into a one-minute discussion on "paramount" and everything like that.
So going forward, Corey, I request that if I ask for a basis just tell me the legal basis, not your reasoning why it's vague, or -- or lack of foundation. Fair enough?
MR. COREY GORDON: I'm not going to agree to --
MR. ASSAAD: Okay. So you don't want to agree to no speaking objections. I understand.
MR. COREY GORDON: I'm not going to agree

to your characterizations.
MR. ASSAAD: Okay.
BY MR. ASSAAD:
Q. So with respect to a medical device, you would agree with me that the responsibility to determine its safety before it goes on the market is the manufacturer of the medical device; correct?
A. Yeah. That's why they fund studies, to test both safety and efficacy.
Q. And they should fund studies; correct?
A. I would hope they would do a lot of funding.
Q. Okay. And if -- if there are researchers in the field that are experts in certain areas and -- and recommend research to a manufacturer regarding the safety of their product, they should take that into consideration in whether or not to do research; correct?
MR. COREY GORDON: Object to the form of the question.
A. So you're asking if industry makes a decision as to who does the study; is that what you're getting at?
Q. No. I'm saying that if there is -- if there is an issue regarding the safety of a product --
A. Yeah.

Q. -- and the recommendation by, say, for example, a -- the advisory -- the Scientific Advisory Board member of -- of a corporation that you need to do some research regarding the safety of this product, do you agree that a responsible corporation would consider doing the research?
A. Yeah. If there was a signal somewhere that the device or a product was unsafe, yeah, they need to go get some more work to prove it one way or another.
Q. You're aware that Dr. Sessler has done a lot of research regarding maintaining normothermia and the Bair Hugger.
A. Yeah, he has. I don't know everything that he's done, I have to tell you that.
Q. Are you aware that he's on the Advisory Board for 3M?
A. I may have seen that in one of the depositions. I wasn't aware of that --
Q. Are you aware that --
A. -- in general.
Q. -- he ghost wrote, or not ghost wrote, he -- he -- I'm sorry -- he submitted a study in 2011 regarding particle tests?
A. I'm not sure I knew that.
Q. Did you not review the 2011 study by -- by

Daniel Sessler and Russ Olmsted?
A. I may have, I just can't recall the study.
Q. Do you know who Russ Olmsted is?
A. No.
Q. So going back to your CV under your bibliography, it seems like you wrote two books, textbooks in 2014 under "Clinical Decision Support"?
A. Oh yeah. That's an online text now, --
Q. Do --
A. -- resource.
Q. Do you consider those authoritative?
A. Yeah.
Q. Okay.
A. I'm biased, but.
Q. Okay.
A. So you need to know that.
Q. Under "Journal/Book Section Editor" you have seven articles there under -- seven -- seven journal/book documents.
A. Where? Where are we?
Q. Right under "Text Books."
A. Oh, okay.
Q. Do you consider those authoritative?
A. If I was involved at the time I did my best to make those accurate.

Q. So you consider those accurate and authoritative?
A. Yeah, at the time that we did it.
Q. Okay. What are "Books For General Readership," are those the two books, your fiction and nonfiction?
A. Yeah. I want you to buy one for everybody in your corporation so that they can have a good time.
Q. Well if you gave me a free copy I may have been able to recommend it.
(Laughter.)
MR. COREY GORDON: I can recommend it.
A. I'll send you a copy later. We'll get you a co --
MR. COREY GORDON: And I -- I paid for mine.
THE WITNESS: I'll give you another one.
MS. ZIMMERMAN: If you're reading anything but literature.
Q. Then, under "Monograph," do you consider those authoritative?
A. Yeah, they were -- you know, they were trying to be up-to-date summaries, they weren't trying to be in any way in-depth sort of critical reviews.
Q. But --

So, for example, under Doebbeling, Herwaldt, Nettleman, Pfaller and Wenzel, "Hospital-Acquired Infections: New Challenges," 1991, do you consider that authoritative?

A. It was at the time.

Where are we, though? I just want to make sure.

Q. Under "Monographs," number 2.

A. Text Books. Oh, I'm sorry.

Yeah. I mean, I did my best at the time.

Q. Who's --

Under "A Guide to Infection Control in the Hospital," "Editors," that one interested me because you write: "Over 60,000 copies have been distributed free of charge --

A. Yeah.

Q. -- to healthcare workers in the developing world --

A. Yeah.

Q. -- countries by the end of 2008."

And by the way, you're missing a space in your CV between "countries" and "by." You might want to fix that.

MR. COREY GORDON: And "countries" is misspelled.

A. Oh.

MR. ASSAAD: Yes, and that, too.

MR. GOSS: Mistakes.

A. Appreciate that.

Q. Was this funded by a nonprofit organization, or --

A. Actually I've been a member of the International Society for Infectious Disease for a long time, and was president roughly, I don't remember, 2008 or '10 or so. And three years before that I was asked by the former president if I would organize a handbook; in other words, something that would fit in a pocket, that would be useful to give to healthcare workers in countries throughout the world that are developing countries that really couldn't afford to buy a text that have no computer resources. So I did that, and the handbook is just what it looks like, about a handbook size.

Q. And you've updated it periodically, you started in 1998; correct?

A. Yeah.

Q. And the last edition was 2008?

A. No. That's the last one that I -- and actually there are -- there are ones I've passed it over to now, a first editor, Gonzalo Bearman, who's at

our institution, and on the last one, which was probably 2014 or '15, I was a senior author or senior editor, if you will. I'm trying to transition to other people. And so for the next one that'll be out in a year or two, I won't be editing that.

Q. But in any event, you consider that authoritative.

A. Well it's very good for what we're trying to do.

Q. Okay.

A. We're trying to provide resources to --

Q. Prevent infections.

A. Absolutely.

Q. So you consider it authoritative and you're sending it around the world.

A. Yeah. No. I mean for -- But it's targeting, particularly, countries that have limited resources, so it's not -- it's not an in-depth review, it's really trying to focus as much as possible on the problems they face.

Q. But you agree with everything in it; correct?

A. Yes, I think so. I've read -- everything that I have put there I pretty much have reviewed.

Q. You're the editor.

A. Yeah.

Q. Okay. And you're the first-named editor; correct?

A. Most of the time there. With all this, yeah.

Q. I mean you were primari --

A. I am now there.

Q. But during this time you were primarily responsible for the book.

A. That's correct, yeah.

Q. Okay. And I assume that you edited and reviewed everything that was in -- in here.

A. I have, yeah.

Q. Okay. And if there's something that you disagree with it you would have objected to putting it in there.

A. Yeah, or if you find something, I'll take it look at it.

Q. Okay. And do you -- do you consider all your publications or papers authoritative?

A. Well given my bias, which I've told you before, --

Q. Okay.

A. -- I'd like to think so.

Q. Whether or not you were the advisor or the

first-named author, you consider it authoritative.
A. Yeah. I read -- I read the papers that I'm involved in, yeah.
MR. ASSAAD: Let's take a break for the court reporter.
THE WITNESS: Okay.
THE REPORTER: Thank you. Off the record.
(Recess taken from 10:18 to 10:31 a.m.)
(Discussion off the stenographic record.)
BY MR. ASSAAD:
Q. You mention --
We talked about particles briefly, in -- in the operating room, and that they can carry bacteria.
Do you agree with me that the reduction of airborne particles in an operating room is beneficial?
MR. COREY GORDON: Object to the form of the question.
A. So I haven't seen any data to show the reduction in airborne particles actually reduces infection rates with maybe, you know, one exception, the Darouiche study that's more recent where he looked at particles in bacteria and he modeled particles in bacteria and said that they correlate, but he actually didn't show, in a prospective way, that they reduced infections because he didn't do any microbiology. So

there might be a signal out there, but I'm not aware of any study that said if I took out Staph -- now you're just talking about particles maybe, I'm sorry, maybe I'm mixing this up -- but if I reduce particles that I would have fewer infection rates. I think that's what a lot of the laminar flow studies actually showed didn't occur.
Q. So I'm guessing your opinion --
A. Yeah.
Q. Do you have an opinion whether or not the -- the number of particles over a surgical site have an effect on surgical-site infections?
A. So I guess I would say it this way. If I knew that there was a hundred percent sort of particle to bacteria, I'm more interested in bacteria than I am particles. They're both surrogate markers for what really is going on. What we really want to know is what can we do to stop the endpoint, surgical-site infections. And so then there are some studies that have tried to say, if I have particles, you know, I have bacteria. Not all studies have really shown the same thing always, so there's some discrepancy between the relationship of particles and bacteria. And again, the second part of that is if you have bacteria and -- do they cause the infection.

Q. Okay. So my question is again, do you have an opinion -- do you have an opinion whether or not the number of particles over a surgical site have an effect on surgical-site infections; "yes" or "no"?
MR. COREY GORDON: Object to the form of the question, asked and answered.
A. Yeah, I think what I'm trying to do is give you the best answer I can, you know, --
Q. Well --
A. -- that, you know, we don't have complete data yet to really say that particles equal infections.
Q. Okay. So you're not saying that particles do not equal infections, and you're not saying that particle -- increased particles increase infections, you're just saying that there's not enough data.
A. Yes.
Q. So my understanding is you don't have an opinion at this point in time whether or not the number of particles over a surgical site increase the risks of surgical-site infections.
MR. COREY GORDON: Object to the form of the question.
A. I don't think there are data to say that if you have a certain number it's going to predict an

infection.
Q. So you have no opinion at this time.
A. Well that's my opinion.
Q. Well your opinion is that there's no data.
A. Yeah. We need more data.
Q. Okay. So your opinion is you don't have an --
Okay. Do you agree that if you increase the number of particles you increase the risk of surgical-site infection?
MR. COREY GORDON: Object to the form of the question.
A. Yeah, I don't think -- I don't think there are data that really show that, so.
Q. So you don't agree with that.
A. Yeah.
Q. So you don't agree with that.
A. I don't agree with it.
Q. Do you agree that you if you reduce the numbers of particles you decrease the risk of surgical-site infection?
A. And again I've cited the studies from the laminar airflow would clearly reduce the number of particles, didn't reduce the number of infections.
Q. So you don't agree with that.

A. That's right.
Q. Okay. So you don't agree that if you reduce the number of particles over the surgical site, you don't reduce -- you don't reduce the --
A. Yeah, I think we have firm evidence on that.
(Interruption by the reporter.)
THE REPORTER: So you don't agree that if you reduce the number of particles over the surgical site?
Q. -- you reduce the risk of surgical-site infections.
A. Yeah. The only signal that I would even point to would be Darouiche.
Q. Do you consider Darouiche an expert?
A. I think he's done really good work, yeah. So I think he's good.
Q. So you consider him an expert?
A. Yeah.
Q. You do understand that hospitals spend a significant amount of money to reduce the particle load in an operating room.
MR. COREY GORDON: Object to the form of the question.
A. Say that again if you would.
Q. Hos --

I mean, you understand that there is an HVAC system in the operating room; correct?
A. Yes.
Q. And it's -- there are -- there are standards in many states regarding the type of filtration to be used in an operating room.
MR. COREY GORDON: Object to the form of the question and lack of foundation.
A. I -- I think there are standards.
Q. Have you heard of ASHRAE?
A. Yes.
Q. Okay. And you understand for an operating room, most operating rooms contain two filters?
A. Yeah, I think they're MERV 14 or something like that.
Q. It's a MERV 7 for the prefilter and the MERV 14 for the final filter. Do you --
Have you heard that before?
A. I've heard the 14.
Q. Okay. And you understand the purpose of that is to reduce the number of airborne contaminants in the operating room; correct?
A. Yes.
Q. Okay. And you agree with that; correct?
A. I do.

Q. Okay. And you understand that in an operating room they control for humidity to limit the amount of bacterial growth.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, I don't know the relationship to humidity.
Q. Okay. So you're not -- you don't -- you have done no research or have no understanding how humidity affects bacterial growth?
A. True.
Q. Okay. And you're not an expert in filtration; correct?
A. No, only in the sense I don't want to completely -- if you're talking about all filters and nothing to do with infectious diseases, where they interact I think I can make an opinion. But no, I'm not an expert just in filters.
Q. You agree that the cleanest air that's coming into the operating room is coming through the vents.
MR. COREY GORDON: Object -- Object to the form of the question, and lack of foundation.
A. You mean the filtered air is cleaner than somewhere else?

Q. Yes.
A. Yeah.
Q. Where do you think the greatest bioburden is in the operating room?
A. I just saw a bioluminescence study that says the side of the table, I think, in one study. And I'm not an expert in where the greatest bioburden is, but so that's the recent study that looked like that.
Q. Side of the surgical table?
A. And the computer, actually, was very -- was very high numbers.
Q. But the computer is outside of the -- the sterile field; correct?
A. It's --
MR. COREY GORDON: Object to the form of the question.
A. -- outside the sterile field.
Q. It's behind the surgeons actually; correct?
A. Yeah.
Q. Do you agree that there is a significant amount of bioburden around the surgical table and underneath the surgical table?
MR. COREY GORDON: Object to the form of the question.
A. So in that one study that I saw with the

bioluminescence is the only data that I know about burden.
Q. Okay. So you only rely on literature and not on any type of scientific reasoning that you could draw from that literature?
MR. COREY GORDON: Object to the form of the question.
A. So I'm not sure of the difference. I mean I would have said the literature -- You read the data, and then you interpret the data based on maybe a host of other studies, and together you come up with an opinion.
Q. I understand that. But sometimes you want to do research and you'll have a hypothesis; correct?
A. Yeah. I'm not sure how that relates to the earlier question.
Q. Well I'm saying, like, well you know that the air coming out of the vents is filtered air; correct?
A. Yes.
Q. And you know that there is many people in the operating room around the surgical table; correct?
A. Yeah. Yeah.
Q. There is the patient; correct?
A. Yeah.

Q. There is probably two or three people performing the surgery in an orthopedic surgery; correct?
A. Yes.
Q. And there is an anesthesiologist; correct?
A. Yes, there is.
Q. And they are shedding skin squames; correct?
A. Yeah. People who have studied that said yeah.
Q. Do you disagree with that?
A. No.
Q. Okay. And therefore, you would agree with me that the airflow is pushing down the skin squames to the floor area; correct?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. Well I don't know that the airflow is only pushing things down to the floor. I don't know that.
Q. Okay. So sitting here today you don't know where the greatest bio -- like where the greatest bioburden is in the operating room, in the air of the operating room?
A. No, --
MR. COREY GORDON: Object to the form of the question.

A. -- the only study is the one I cited.
Q. Okay.
A. And you know what I'm talking about, Richard?
Q. Yes.
A. Yeah.
Q. Now you do understand that the surgeons and the staff in the operating room are trained not to put their hands below the operating room table.
A. I think that's right.
Q. Why is that?
A. I think that they just try to keep things right near the field, that's my -- I'm guessing a little bit on that, but.
Q. So as an infectious disease person you don't understand why they -- they want to keep their hands -- they're trained to keep their hands always above the operating room table?
A. Well I think they don't want to touch the side of the table.
Q. Yeah, but they're not evened allowed to put their hands down, and not touch anything.
MR. COREY GORDON: Object to the form of the question.
Q. Do you agree with that?

A. Yeah, I don't -- I can't say I've seen rules for that or anything, and you may be right.
Q. Okay. So you don't know -- you don't -- you haven't read any literature on -- or strike that.
You haven't looked at procedures or been involved in any training discussing --
A. Where they hold their hands.
Q. -- or training nurses -- or nurses and surgeons to keep their hands above the operating room table to avoid for their hands to be contaminated.
A. I didn't do any research on that, I haven't --
Q. Okay.
A. -- seen it.
Q. By the way, before getting involved in this case did you do -- did you know anything about the Bair Hugger?
A. The only thing I knew was the Kurz study was pretty much it.
Q. The 1996 New England Journal of Medicine?
A. That's right.
Q. Okay.
A. I may have read Melling, but, you know, I just remember the Kurz study.
Q. Do you know what the difference between the

Melling study and the Kurz study is?
A. I do.
Q. What's the difference?
A. Well in the Kurz study the authors randomized 200 patients who were undergoing colorectal surgery to warm air with the Bair Hugger, to ambient air, it was double blind study as a result of the -- using the ambient air, and the outcome was surgical-site infections. I'm not sure if you want to know any more about that.
Melling, which was published in 2001, actually took patients who were expected to have a surgical time of about 50 minutes or less --
(Interruption by the reporter.)
THE WITNESS: Fifty, five-oh.
A. -- they were clean surgery, there were 421 patients who were randomized. What was different was that they pre-warmed the patients for 30 minutes or more, and... And again, just like the Melling, they showed a 3-to-1 ratio, three times the risk of infection in the warmed patients versus the non-warmed patients. And I want to point out the consistency of that 3-to-1 ratio.
Q. Okay. So you do understand that Melling was pre-warming; correct?

A. Yes.
Q. Okay. It wasn't perioperative warming.
A. That's correct.
Q. Okay. And I'm sure you're aware of studies that -- recent studies done by Dr. Sessler and others, that forced-air warming has very little effect on core temperature for the first hour when you're warming perioperatively.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, I don't -- I don't know that it has no effect or very little effect in the first hour.
Q. Well you're aware of those studies; correct?
A. I remember hearing --
MR. COREY GORDON: Object to the form of the question.
A. -- about but I just can't cite them.
Q. Okay. So you're not going to -- I mean --
Well you understand that Kurz was 1996; correct?
A. It was 1996.
Q. And you understand that Kurz actively cooled patients for the control.
MR. COREY GORDON: Object to the form of the question.

A. Kept them at ambient air, yes.
Q. Well they didn't keep them am -- They blew ambient air --
A. Blew ambient air, --
Q. -- which would be
A. -- hooked them up ambient air.
Q. Which would be a cooling effect on a patient; correct?
A. Yes.
Q. Okay. That would be unethical today; correct?
A. Every -- With the effect of warming, particularly warming a surgical-site infections, nobody should go to the operating room without being warmed.
Q. But you would -- you agree you wouldn't be able to do a study and cool patients today.
A. No, no. That's what I'm saying.
Q. You could be --
A. They have to be warm.
Q. Okay. And -- And Melling was pre-warming; correct?
A. Melling was pre-warming. But there are data to show that the pre-warming actually last up to three hours. I've cited that in my report.

Q. Okay. And that's a good thing; correct?
A. I think it's a good thing.
Q. So you would agree with me that, for example, total hip and total knee arthroplasty, that you could just pre-warm a patient because its effects are for three hours and most of the surgeries last below three hours.
A. I don't know anybody --
MR. COREY GORDON: Object to the form of the question.
THE WITNESS: I'm sorry. I didn't mean to interrupt, Corey.
A. I don't know anybody who's totally done pre-warming with total hips and knees, if that's what you're asking.
Q. You agree with me that there's no study out there that -- that looked at the -- the effects of warming a patient and periprosthetic joint infection.
A. That's not quite accurate, because what I've done is show some cohort studies, if you want to refer to those in my report.
Q. Can you just give me the name of the study?
A. So the --
Well the first was -- I have a chart actually in my report. On the top of the chart it

will say there's a study from Hopkins, there were fi -- I think I had six -- five or six cohorts. There was a second study that was done by Leijtens in Denmark, and that was total hips and total knees.

Q. Which is the chart you're referring to?

A. Is this my report? Yeah. (Witness reviewing exhibit.) So page 8. So let's look at -- under number 2, this was by Leijtens, it was done in Holland, total hips and knees. And what they show -- They -- These people addressed the question, to put it in perspective, if patients were warmed or -- you know, during the operation compared to those who remained hypothermic, was there a difference. And as you can see, there is a risk ratio of being cool of 3.7. And I would point out again that if you look at Melling or you look at Kurz, it's about three times the risk of infections --

Q. But the P value --

A. -- if you're cool.

Q. P value is .061; correct?

(Interruption by the reporter.)

A. .061.

THE WITNESS: I'm sorry.

Q. And you agree with me that the only infections were in total hip and not in the total

knee.

A. I don't remember. I think that's probably right, but I don't remember.

Q. Okay. And basically there was four out of 109 that were hypothermic, and three out of 306 that were normothermic; correct?

A. Yeah, I don't have it in front of me.

Q. Okay.

A. But I've said seven -- I have in the chart 27 percent total.

Q. Okay. And --

A. And nobody, by the way, with that .06 is going to discard that. If you were having hip surgery and you were in Holland and you -- and I'm telling you you have three times the risk plus if you weren't warmed, are you going to argue with me as a patient say the P was only .06? I don't think so.

Q. You agree with me that all the patients were warmed with the Bair Hugger in that study.

A. They were Bair Hugger.

Q. And all of them were warmed; correct?

A. Did you say all of them were warmed?

Q. I mean they all were warmed with the Bair Hugger device.

A. That was the -- As far as I understand,

yeah.

Q. And so basically for a significant number of them that were warmed with the Bair Hugger, they still became hypothermic; correct?

A. That's correct.

Q. Okay. So that might indicate that there might be something else besides warming a patient that affects hypothermia.

MR. COREY GORDON: Object to the form of the question, lack of foundation.

A. Say that again to make sure I follow you.

Q. Well they were all warmed with the Bair Hugger; correct?

A. They were. They were.

Q. And even though you were warmed with the Bair Hugger, a significant amount of patients, 27 percent, became hypothermic; correct?

A. That's correct.

Q. Okay. So it is possible that there's something else besides warming that caused hypothermia.

MR. COREY GORDON: Object to the form of the question.

Q. That's a bad question.

The patients became hypothermic even though

they were warmed.

A. That's easier to answer, yeah. And I have the -- the 27 percent. That's the figure I reported.

Q. So you weren't comparing the use of Bair Hugger versus the non-use of Bair Hugger with respect to infection rates in that study; correct?

A. Only the endpoint, whether you were warmed with the Bair Hugger versus not warmed.

Q. So you could have been warmed with a -- a convective blanket in that case; correct?

A. They weren't, but if you're asking me as long as the patient's warmed, do you think they'll do better?

Q. Okay.

A. That hasn't been done. I'd love to see a HotDog versus the Bair Hugger studied.

Q. You've never seen that?

A. Oh. Never seen a straightforward, randomized controlled trial of one versus the other, no.

Q. Okay. You've never seen a study that was authored by -- one of the authors was Andrea Kurz on that study? That wasn't provided to you by the defense?

A. That was the first study you mean?

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Q. No. A study with Andrea Kurz and a few -- and Kimberger?
A. Tell me about this study.
Q. Where they compared the HotDog to the -- the -- the HotDog to the Bair Hugger to see whether or not --
A. In a prospective clinical trial? I don't remember that study.
Q. Do you only count prospective clinical trials?
A. Well in the hierarchy of quality of evidence, to me that's number one.
Q. Some people disagree with that, though; correct?
A. Some might.
Q. Okay. And then we could eliminate number 1, number 3, and number -- and number 4 because they didn't deal with total hip and total knee; correct?
A. Well I don't think I would --
MR. COREY GORDON: Object to the form of the question.
A. Yeah. I don't think I would eliminate number 4 either, because I think they were -- they were orthopedic patients with hip fractures. I don't think that I would say positively they wou -- that

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doesn't have any relevance to --
Q. Well let's look at being warmed and not being warmed, --
A. Yeah.
Q. -- okay? And that's number 5; correct?
A. Yes.
Q. Which is the Frisch study; correct?
A. Yeah. That's right.
Q. And the Frisch study said, hey, it doesn't matter if you're being warmed because 1 percent got infections if you were warmed and 1 percent didn't get it if you weren't warmed; correct?
A. So I put that study in to let you know that --
Q. You disagree with it.
A. -- I looked at all literature and didn't just cherry-pick anything.
Now if I want to look at that study, let's talk about it. Look at the high proportion, for some reason, that never -- that got cool, 43, thirty -- 44 and 33 percent. And there are a couple other weird things. The follow-up was six weeks. So really hard to pick up a lot of deep infections in six weeks. They didn't regulate the temperature in that study in the operating room, as you know. And they did

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something strange. They said, if you were giving logical anesthesia they didn't warm the patients unless the patients became hypothermic.
So a lot of weird things about that study. But the data, I'm trying to tell you, I didn't try to hide anything, I put it in there.
Q. But we're seeing 44 percent were hypothermic.
A. Yeah.
Q. Okay. And -- And -- Of total hip, and 33 percent were hypothermic for total knee; correct?
A. That's right.
Q. Okay. And you saw no difference in infection.
A. That's correct.
Q. Okay. And that was 2017; correct?
A. That's right.
Q. And out of all the studies dealing with total hip and total knee that you've listed, that had the highest number of participants.
A. Don't remember the numbers, but maybe.
Q. You have it right here under number of patients.
A. Oh, okay. I see what you're saying.
Q. You have 600 and --

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A. Yeah.
Q. Okay. You have 2,397; correct?
A. Yeah. Of the hips and anything to do with orthopedics, right.
Q. And you said a study of only looking at six weeks will not pick up deep joint infections?
A. Might miss a lot of them.
Q. Okay. Because they may -- they may occur one year after; correct?
A. Could be, but at least out three months. I don't know why you wouldn't do that.
Q. I mean some of them even occur two years; correct?
A. Some people show up two years later. It's always hard to know, you know, did they have an interim -- intermittent bloodstream infection, but out to a year --
(Interruption by the reporter.)
A. -- intermittent bloodstream infection that landed on the device.
Q. And -- And there are -- there are some case studies out there that indicate that they could have had -- come up and be five years later if there's no intermittent infection. They trace it back to the implant surgery.

A. I've heard that there are case reports like that, yeah. I can't cite any.
Q. But you've heard of it; right?
A. Yeah.
Q. And you don't disagree with it.
A. If it's a real report, it's a real report, that's what happened.
Q. And -- And --
A. But what I'm saying is some -- it's really hard as a clinician, facing those patients, was that patient infected at the time of surgery, just so we're clear, or did they went to the dentist, they have horrible teeth, they had a -- you know, some manipulation in the mouth and they got a secondary bacteremia and they settled on the prosthesis. Five years out you can't tell.
Q. Well you know that secondary bacterium theory is under a lot of dispute.
A. It might be under dispute, but I'm telling you as a clinician standing in front of the patient.
Q. Okay. I understand that, but it's not settled whether or not secondary bacterium from the mouth causes a periprosthetic joint infection. You've read articles --
A. That's the deba --

There's a debate going on as to whether or not these patients should all be screened by their oral surgeons or not beforehand because it's a worry.
Q. Okay. And since you believe that the most likely cause of a surgical-site infection is patient flora, then you would agree with me that the likelihood that the anesthesia machine caused a surgical-site infection is very low.
MR. COREY GORDON: Object to the form of the question.
A. In general I think that's true.
Q. Okay.
A. Would there be an exception, an outbreak or something like that where something happened? Yeah. But that's what I would say in general, yes, I think it's low.
Q. We're talking probabilities here.
A. Yeah. No, I'm with you.
Q. And you agree with me that the probability that a surgical light causes a surgical-site infection is very low.
(Interruption by the reporter.)
A. Yeah, I don't think I've seen any studies related to that.
Q. And you'd agree with me that comput -- the likelihood that computer monitors cause a surgical-site infection, or the fans in them cause a surgical-site infection is very low.

A. Yeah. I haven't seen any data linking them.
Q. Okay. And you agree with me that the computer console and the equipment in them, the likelihood of them causing a surgical-site infection is very low.
A. And again I can't cite any papers that link them, yeah.
Q. So you agree with me.
A. Yeah.
Q. Okay. You agree with me that the electrocautery device itself has a very low likelihood of causing a surgical-site infection.
A. Based on not having any data, yeah.
Q. So you agree with me.
You agree with me that a bovie is very unlikely to cause a surgical-site infection.
MR. COREY GORDON: Object to the form of the question, also I guess that's asked and answered.
A. I just -- Yeah, I just don't know any data with the bovie or the knife or...
Q. You agree with me that sterile surgical drapes are very unlikely to cause a surgical-site infection.

MR. COREY GORDON: Object to the form of the question.
A. I would say that anything sterile is unlikely to cause an infection.
Q. You agree with me that the cabinets along the walls are very unlikely to cause a surgical-site infection.
A. Same answer. I haven't seen any data. I think it's unlikely.
Q. You agree with me that the suction drain that's in the operating room is very unlikely to cause a surgical-site infection.
A. Yeah, I think drains have been known to harbor certain organisms like Pseudomonas, but again, if you say standard procedures that have been, you know, done to try to minimize that, I think it's unlikely.
Q. And when I ask you these questions, doctor, let's just assume that the hospital, the doctors and the nurses are following the standard of care.
A. I'm with you.
Q. Okay.
A. I'll follow that.
Q. Okay. Like, for example --

A. I like infection control, so I'm with you. I'll imagine the perfect hospital.
Q. Okay. Like, for example, we're not expecting a nurse to take off her mask and sneeze right into the surgical site, you know, okay?
A. I would hope so.
Q. Okay. You agree with me that sterilized surgical instruments are very unlikely to cause a surgical-site infection.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, in general again, anything sterile. Now once they're used they're no longer sterile, but, yes, I think that's true, and I agree with you.
Q. Yeah, I understand that when you cut the skin they may no longer be sterile; correct?
A. Yes. That's correct.
Q. However, you do understand that in orthopedic implant surgeries the standard of care is after you make the first incision -- or some surgeons would say after you make the first incision to switch the scalpel.
A. Yes.
MR. COREY GORDON: Object to the form of the question, lack of foundation, assumes facts not

in evidence.
THE WITNESS: Sorry.
Q. The drop buckets for a used sponge, do you agree with me that they're very unlikely to cause a surgical-site infection?
A. Again I'll say the same thing, you know, I don't know any data, so I think it's low probability.
Q. And same question with the trash receptacle. You agree with me the trash receptacle is very unlikely to cause a surgical-site infection.
A. Yes.
Q. And do you agree with me that surgeons moving their hands is very unlikely to cause a surgical-site infection?
MR. COREY GORDON: Object to the form of the question.
A. So a surgeon doing surgery is moving his hands.
Q. He's moving his hands like this [demonstrating].
A. Yeah. And is that a cause, assuming that nothing else is happening? Yeah, I don't think the movement of hands. Now people talk about the movement of hands creating more particles and whether that's linked, we talked about that earlier. It's hard to

show a link with particles and surgical-site infections.
Q. Have you read Dr. Mont's expert report?
A. Yes, I did look at that.
Q. Okay.
A. Yeah.
Q. Do you criticize anything in his report?
A. Yeah, I don't think I saw anything that I'd criticize.
Q. Okay. Do you believe that -- Have you read --
Have you read all the defense expert reports, all the -- all 12 others?
A. No, I don't think I read 12.
Q. Okay. Have you read Dr. Ho's expert report?
A. No, I didn't see that.
Q. Have you read Dr. Kuehn's expert report?
A. No.
Q. Have you read Dr. Abraham's expert report?
A. No.
Q. So what expert reports have you read? Dr. Borak?
A. Borak, Holford.
On this side of the table you mean?
Q. Yes.

A. Mont. I'm not sure who else. I think that -- that may be it, I don't remember.
Q. Have you met Dr. Mont?
A. Just at Science Day is the only time.
Q. Have you met anyone from 3M in preparation of your expert report?
A. No.
Q. Have you not met Al Van Duren?
A. No.
Q. Have you read Al Van Duren's deposition?
A. No.
Q. You haven't read his 30(b)(6) deposition?
A. No.
Q. Do you know what a 30(b)(6) --
A. No, --
Q. -- deposition is?
A. -- have no idea.
Q. So have you --
Have you read Gary Hansen's deposition?
A. No.
Q. Have you read any other --
Have you read any other depositions besides expert depositions?
A. No, I don't think so.
Q. Well that's not exactly true, --

MR. COREY GORDON: Yeah.
Q. -- and I apologize for that.
MR. COREY GORDON: Kurz and Sessler.
A. Oh, I'm sorry.
Q. You've read the depositions listed in Exhibit --
A. Yeah. I'm sorry. I didn't -- I thought you meant from 3M or something.
Q. Exhibit, I think it's 3?
MR. COREY GORDON: 2.
Q. 2.
So besides these depositions listed in Exhibit 2, what other depositions -- Strike that.
You've read Holford, Borak and Mont. Any other depositions you reviewed that are on the defense side?
A. I don't -- I don't think so. I don't recall any other ones.
Q. You actually -- Before I get there.
And you've read the depositions of plaintiffs' experts; correct?
A. I read Jarvis, Samet, and I think I've read Augustine.
Q. You think Augustine is on the plaintiffs' side?

A. Oh, I'm sorry. I don't --
Do I think he's on the plaintiffs' side? I thought so.
Q. Why did you think that? Did someone tell you that?
A. No. I mean, he -- he is in charge of the company making the competitor.
Q. Well there's a lot of competitors, aren't there?
A. Well I think that's the key one we're focusing on if we're really going to be talking man to man here. That's the one that's --
Q. Let's talk man to man.
A. Yeah.
Q. Let's talk man to man.
(Laughter.)
MS. ZIMMERMAN: I'm going to excuse myself for this.
(Laughter.)
THE WITNESS: I'm sorry. I meant that as kind of a joke.
Q. So, I mean, have you heard of VitaHEAT?
A. No, I don't --
Q. VitaHEAT was a competitor of 3M that 3M just bought. Are you aware of that?

A. No, I didn't.
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence.
THE WITNESS: Sorry.
Q. Are you aware of Mistral?
A. No.
Q. Are you aware of WarmTouch?
A. I've heard of WarmTouch, yeah.
Q. Okay.
A. I think WarmTouch is what they use at Hopkins.
Q. Okay. So there's other forced-air warming devices as well as convective devices; --
A. Yeah.
Q. -- correct?
A. Yeah.
Q. Okay. And you're aware that, you know, other competitors of 3M have done research to compare their product to the Bair Hugger.
A. I don't -- I mean, the only ones I've seen have really been the HotDog and, you know, and, let's say, Augustine's new study which I don't know if it's --
Q. I don't want to talk about that today.
A. -- it's on the table or not, but yeah.

Q. I mean, there's -- there's Warm --
A. And the McGovern study I mean obviously is the big study you have for your side of the table.
Q. Well is that what someone told you?
A. Not --
Are you asking me if someone told me that?
Q. I mean -- I mean, you say you thought --
A. Why do I say that?
Q. -- you thought Augustine was on the plaintiffs' side. Why would you make that assumption?
A. Because he compared, you know, his product to the Bair Hugger in the new study --
Q. You're aware that --
A. -- which you don't want to talk about, but.
Q. You're aware that Augustine invented the Bair Hugger; correct?
A. I do, yeah.
Q. Okay. So do you criticize any of his older studies that he did on Bair Hugger before he left Arizant?
A. I don't know if I know all of his old studies, but I think -- you know my opinion. I think the Bair Hugger works, I think there are no data out there to definitively link it to harm.
Q. Well we have two studies that you just

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indicated that you -- that it support your opinion that Bair Hugger works for total hip and total knee. One said it doesn't make a difference, --

A. Umm-hmm.

Q. -- and the other was where they compared Bair Hugger -- and one where the Bair Hugger was used all the time and indicated even when you used the Bair Hugger that it didn't maintain hypothermia; correct?

MR. COREY GORDON: Object to the form of the question, mischaracterizes his testimony, --

Q. Isn't that what those studies say?

MR. COREY GORDON: Let me finish my objection, please.

MR. ASSAAD: Okay.

MR. COREY GORDON: -- misstates the evidence, form.

Q. We can go back if you want, doctor. Do you want to go back? Let's go back.

A. Let's do that. That'd be fine.

Q. Let's be 100 percent correct what these studies say.

A. Yeah, that's fine.

Q. Because we want to be accurate; correct?

A. Yes.

Q. We don't want to be an advocate for the

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defense. You want to be --

A. I'm not an advocate.

Q. You want to be objective; correct?

A. Yes. That's --

Q. Okay.

A. That's good.

Q. Being objective is really important when thousands of people's -- of lives are at stake; correct?

A. Yes.

Q. Okay. And what page are you looking at, sir?

A. Page 8.

Q. Okay. So let's look at the two studies that dealt with total hip and total knee.

A. Yep.

Q. Okay. One was the one in Holland; correct?

A. Yes.

Q. Where Bair Hugger was used on all the patients; correct?

A. Yes. That's my understanding.

Q. And even when the Bair Hugger is used, 27 percent of the people still became hypothermic; correct?

A. That's correct.

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Q. That would indicate that the Bair Hugger may not maintain normothermia during a surgery; correct?

A. For that study that's correct.

Q. Okay. And that looks -- And that showed a 3.7 percent if they were --

A. No, not "percent." It's a risk ratio.

Q. You have percent there, sir.

A. Oh, I'm sorry. It's both.

Q. Okay. And one per -- if they're hypothermic; correct?

A. Yes.

Q. So there might be something else in the oper --

MR. COREY GORDON: I think you misstated that.

MR. ASSAAD: I don't think I misstated it.

MR. COREY GORDON: You said one percent if they're hypothermic.

MR. ASSAAD: I said -- I thought I said "warmed." Did I say --

A. One percent if warmed, versus 3.7 if hypothermic.

Q. Okay. And the p value was -- would indicate to many people out in the research field that it's not

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statistically significant; correct?

MR. COREY GORDON: Object to the form of the question.

A. I think many people who are out there would not blow this off at .06.

Q. They would do further studies, wouldn't they?

A. Well they probably would do further studies, yes. But I think no one would discount that is what I've told you earlier if I were advising a patient and that's all we had.

Q. Okay. But we could agree with this study on number 2, the Holland study on Exhibit 1, page 8, that the Bair Hugger, even when used, still may not maintain normothermia; correct?

A. That's true.

Q. Okay. And then let's look at the study that indicate that when the Bair Hugger is used and not used; correct? And we see that when the Bair Hugger is used --

A. Which study are you on?

Q. Number 5, the Frisch study.

A. Okay. Yeah.

Q. Okay.

-- there is a 1 percent infection rate;

correct?
A. Yes.
Q. And when the Bair Hugger is not used there is a 1 percent infection rate; correct?
A. Yes.
Q. Okay. So the Frisch study indicates that -- the Frisch study actually tested the infection rates when the Bair Hugger is used as compared to when the Bair Hugger is not used; correct?
A. Used versus not used?
Q. Yeah.
A. Well they looked at who got cool with the Bair Hugger versus who didn't get cool with the Bair Hugger.
Q. You mean warm.
A. Huh?
Q. You mean warm.
A. Warmed. I'm sorry.
Q. We're not cooling with Bair Huggers; are we?
A. We're what?
Q. We're not cooling with Bair Huggers.
A. No, no. I'm sorry.
Q. Okay. That would be unethical; correct?
A. No, but the percent --
What I'm saying is, you know, they had the

percent here who were under 36 degrees, no question, in a high proportion, unusually high proportion. A lot of strange things which I've already documented about this study. But that's what they showed; no difference, one percent at face value.
Q. And every -- every study has limitations; correct?
A. Every study can be looked at carefully.
Q. Okay. And if you're an advocate you're going to discredit the studies and look at their limitations, and if you're an advocate for a side you're going to not look at the limitations.
A. Well --
MR. COREY GORDON: Object to the form of the question.
A. -- I don't think that's true.
Q. Okay.
(Interruption by the reporter.)
(Discussion off the stenographic record.)
BY MR. ASSAAD:
Q. So going back to what depositions you've read, you've been working on this case for -- since 2015; correct?
A. I think that's right.
Q. Okay. So over -- almost --

A. Two years.
Q. -- two, two and a half years; correct?
And you actually have seen internal documents from 3M; isn't that true?
A. I don't know what documents you're talking about.
Q. I mean, you've read depositions in the Walton case.
A. Oh, I have seen those. Is that what you mean by that?
Q. Yes.
A. In the Walton case, yeah.
Q. And you --
And you've read depositions and you've had internal documents provided to you in the Walton case.
A. Yeah, I haven't looked at Walton for, you know, almost the two years so I can't remember all the things I looked at or not, but I had certainly read everything that I could get my hands on and that they sent.
Q. Okay. And were you told not to include any of the -- any internal documents --
A. No.
Q. -- in -- in your report?
A. No.

Q. Okay. When'd you start writing your report?
A. I tend to not wait till the last second, so I probably started, I'm going to estimate, even a year ago, you know, just to fill out the general areas, you know, what data were available from clinical trials, pretty much trying to look at the hierarchy of the clinical quality, so then I had cohorts, case-control studies and if I learned anything more, and then eventually increased the size of the tables if I was making a table.
Q. So you're telling me the report that you wrote in Walton --
A. Oh, Walton, way back when.
Q. Did you not use any of that report in this report?
A. Yeah, there probably were some same things in terms of the background, some of the same studies, but I think I kept finding more and more studies is all I'm saying, in more recent time.
Q. I understand that, but you started working on this report probably during Walton; correct?
A. Yeah. That's fair.
Q. Okay.
A. I mean I did a report for Walton, and then, you know, when I was asked to make comments there was

only one patient.
Q. And this was on May 29th, 2015.
A. It was way back.
Q. Okay. And you didn't start all over in this case; did you?
A. No. I had the basic -- a basic report for Walton, that's true.
Q. Okay. All right. And so you've been working on this report since early of 2015.
A. Yeah, you could say that.
Q. I mean, your Walton report is -- is approximately 40 pages; --
A. Umm-hmm.
Q. -- correct?
Does that sound about right?
A. I don't remember, but that's about right, yeah.
Q. Okay. Have you compared your Walton report to -- to your current report which is Exhibit 1?
A. I -- I haven't gone back and tried to look line by line or area by area. My guess, it comports to similar things.
MR. ASSAAD: I only have one copy of this, but let's mark this as Exhibit Number?
THE REPORTER: Five.

(Discussion off the stenographic record.)
(Wenzel Exhibit 5 marked for identification.)
(Discussion off the stenographic record.)
BY MR. ASSAAD:
Q. I represent to you that Exhibit Number 5 is a copy of part of your Walton report that indicates the materials that you reviewed in preparation of the Walton report. Does that look familiar?
MR. COREY GORDON: Object to the form of the question, mischaracterizes the document.
A. I don't remember this at all, no.
Q. Can I see that document real quick, because I only have one copy?
A. Yeah, sure. (Handing.)
Q. Do you recall reading the depositions of any of those individuals during the Walton case?
A. I actually don't remember any of that, no. Can't recall.
Q. Can I have it again, sir?
A. (Handing.)
Q. Did you look at medical records in the Walton case?
A. I did.
Q. Okay. Did you ever look at the operating

manual for the Bair Hugger Model 750?
A. I think I looked at that some time ago. I don't remember much about it, but.
Q. It's not listed in Exhibit 1 anywhere.
A. Yeah.
Q. Or in the documents that you considered.
A. I may have looked at that with the Walton case or something way back when, but I just don't remember.
Q. Do you remember receiving many internal documents, as indicated here in Exhibit 5, from 3M?
A. I just can't recall that, so I don't know. Yeah.
Q. Well what's been provided today, --
A. Yeah.
Q. -- are those all the documents that were provided to you by any of the attorneys for 3M, from Blackwell Burke or from Greenberg Traurig?
MR. COREY GORDON: Object to the form of the question.
A. I think I was focusing on sort of this general type of causation question. Was there anything from Blackwell? I don't know.
Q. Did you re --
So you're sitting here today, you didn't

rely on any of the documents, internal documents from 3M.
A. No. I mean I told you what I have, and...
Q. Okay. Well this is what you have for the multidistrict litigation; correct?
A. Yes.
Q. Do you have another file or box of documents that you had for Walton?
A. I don't have anything that I remember a separate file. I mean, my office looks like a mess right now, but --
Q. You do understand the Walton case is still going on.
A. I don't know anything about where it is.
Q. Okay. So have you destroyed them?
A. No.
Q. Okay. So you believe you still have them, you just don't know where they are.
A. Yeah.
Q. Okay. So my understanding is that the expert report of Nurse Hughes was never provided to you; correct?
A. That's true.
Q. And did you review the expert report of Dr. Mont?

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MR. COREY GORDON: Objection, asked and answered.
MR. ASSAAD: I asked him about the deposition.
MR. COREY GORDON: The deposition?
MR. ASSAAD: Yeah. I'm asking about the report this time.
MR. COREY GORDON: You mean the transcript that didn't exist until about an hour ago?
MR. ASSAAD: The expert report.
MR. COREY GORDON: That was -- That was asked and answered.
MR. ASSAAD: Well let me ask it again, because I don't -- I was going through this list and it's not on this list.
MR. COREY GORDON: That's fine.
MR. ASSAAD: It's not worth fighting about.
MR. COREY GORDON: No, it isn't.
A. No. I remember most reading -- most recently reading the -- I guess it's the deposition.
Q. So you've never seen the expert report of Dr. Mont.
A. I think... I'm not sure, okay?
Q. Well if it's not listed in your --
A. Yeah.

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Q. -- in Exhibit 2, --
A. Yeah.
Q. -- then you most likely didn't receive it.
A. Yeah, I don't -- I don't recall it, that's all.
Q. You didn't receive the expert report of Dr. Keen; correct?
A. That's true.
Q. You did not receive the expert report of Dr. Kuehn; correct?
A. Correct.
Q. Or Kuehn [keen]. I say Kuehn [coon] just to distinguish between the two.
A. Okay. Yeah.
Q. You didn't receive the expert report of Dr. Settles; correct?
A. Yes. True.
Q. You did not receive the expert report of Dr. Abraham; correct?
A. That's true.
Q. Okay. Did you see any of the vid --
You said you saw the videos of what Abraham prepared at Science Day; correct?
A. Yeah.
Q. Did you ever review those again?

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A. No.
Q. Did you ever go online to review them?
A. No.
Q. Have you ever been to any of the websites prepared by Blackwell Burke to -- to do a -- a marketing campaign of the benefits of forced-air warming?
MR. COREY GORDON: Object to the form of the question.
A. I don't remember doing that, no.
Q. Are you aware that Blackwell Burke is trying to influence the jury in Minnesota?
MR. COREY GORDON: Object to the form of the question, move to strike.
A. I'm not aware of that.
Q. Okay. Are you aware of any law firm that's representing a manufacturer of a medical device that actually puts out a website and promotes the -- and markets the medical device on their own -- on the website?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. So --
Q. Are you aware of that, "yes" or "no"?
A. So say it again. Just want to make sure I

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understand.
Q. Are you aware of a law firm that actually markets a medical device for a company?
A. No, I'm not.
Q. Okay. You're not a -- You're not familiar with how particles move in airflow; are you?
A. No.
Q. Okay. Have you been provided the expert report of Dr. Lampotang?
A. No.
Q. Do you know who Dr. Lampotang is?
A. No, I don't.
Q. Well do you know who Dr. Mont is?
A. Dr. Mont, yes.
Q. Okay.
A. I met him at --
Q. Science Day.
A. -- Science Day.
Q. Are you --
Do you know any of the experts, like besides Science Day in this -- in this case?
A. You mean like Holford?
Q. Yes.
A. Just met him once.
Q. When?

A. There was a meeting in Washington that counsel was there and Jonathan -- blanking on his last name now.
Q. Borak?
A. -- Borak was there, yeah.
Q. So it was you --
A. That's the first time that we met for a couple hours in Washington.
Q. It was you, Dr. Borak and Dr. Holford?
A. Yeah.
Q. Any other experts?
A. No.
Q. Was that the first time you met Dr. Borak?
A. It was.
Q. Was it the first time you met Dr. Holford?
A. It was.
Q. Do you know Dr. Hannenberg?
A. What's the name?
Q. Do you know Dr. Hannenberg?
A. No, I don't.
Q. Have you looked at the expert report of Dr. Hannenberg?
A. No.
Q. What about Dr. Ho?
A. No.

Q. You haven't seen his expert report; correct?
A. I have not.
Q. And what about Ulatowski; have you seen his expert report?
A. Who?
Q. Ulatowski?
A. No.
Q. At the time of the meeting in Washington, D.C., what did you three discuss?
A. Pretty much that Holford, who's a professor of statistics, was going to look at the statistics part of the McGovern study. And then I had a draft of my own report, I don't know that I brought it, but I said I would send that to the other two to give them sort of background on where my thinking was. And then Dr. Samet --
Q. Dr. Samet or Dr. Borak?
A. I'm sorry. I'm sorry. Dr. Borak.
MS. ZIMMERMAN: Both are Jonathans; right?
THE WITNESS: Yeah, that's right.
A. So Dr. Borak was particularly interested in looking at the rivaroxaban issue, which we consider a confounding problem.
(Interruption by the reporter.)
THE WITNESS: Confounding issue in the

McGovern study.
Q. Dr. Borak was to look at that?
A. Yeah.
Q. So you would defer to him for his analysis of that?
A. Not necessarily, but I think he added something.
Q. You don't --
You wouldn't disagree with him; correct?
A. That's true.
Q. Okay. And you wouldn't disagree with Dr. -- what Dr. Holford has in his report.
A. Yes. I said that, yeah.
Q. Okay. Have you actually looked at a Bair Hugger?
A. I have actually.
Q. When?
A. Well, a couple times. One, Corey has one in his office, but --
Q. In Minneapolis?
A. Huh?
Q. In Minneapolis?
A. In Minneapolis, yeah.
And then I asked a friend of mine, I don't know, maybe a year and a half or so ago, roughly,

who's a thoracic surgeon to walk me through the operating room to see the pre- and post-op and talk about the use of the Bair Hugger warmer which we use.
Q. Do you think using the Bair Hugger as a office warmer using it off label?
(Laughter.)
A. I don't know about that.
MR. COREY GORDON: You have no idea what goes on in my office.
Q. Well have you -- have you -- I mean, have you checked -- have you done any swabs on Corey Gordon's skin to see if he has a higher bioburden than anyone else?
A. I don't really have to answer that, do I?
(Laughter.)
Q. If you did, I really want you to answer it.
(Laughter.)
A. I like your sense of humor.
MR. GOSS: Kind of like walking next to pig pen.
(Laughter.)
MR. COREY GORDON: I don't get no respect.
Q. Did you --
Did you look at the Bair Hugger device with a blanket attached?

A. Yeah.
Q. Okay.
A. Yeah.
Q. And have you felt the air coming out of the -- underneath the blanket?
A. Yeah, you can feel it, yeah. Getting -- The warmth, you mean.
Q. Yeah.
A. Yeah.
Q. You agree that the temperature of the air coming out of the blanket is warmer than the body temperature.
A. I think it is. I mean, it's set at, like, 42, 43, and --
Q. I mean, because if the air coming out was below body temperature it would actually cool the patient; correct?
A. It would cool the patient.
Q. Okay. It would be ridiculous to think that the air coming out of the Bair Hugger is below body temperature; correct?
A. Yes.
These are getting tough now, these questions.
Q. They are, aren't they?

Well there's some experts believe, on the defense side, that the air coming out of the Bair Hugger is less than 36 degrees.
MR. COREY GORDON: Object to the form of the question, that mischaracterizes the evidence, misstates the evidence.
Q. Because that would be ridiculous to think that you'd blow cold air on a patient. That would be unethical. Correct?
A. These days what we know now, yes.
Q. Okay. Now you didn't rely --
Looking at Exhibit 5, in formulating your opinions in this case you did not rely on any of the internal documents provided to you during the Walton case; is that fair?
A. That's true.
Q. Okay. And in fact would it be fair to say that you probably haven't looked at those documents provided to you in Walton since 2015?
A. That's probably true.
Q. Okay. So if I asked you what documents are in that set, you would have no idea.
A. That's probably right.
Q. Okay. Do you believe that 3M gave you all the information necessary to formulate your opinions

in this case?
MR. COREY GORDON: Object to the form of the question.
A. I didn't rely on 3M to provide me all the information. I really did much as I can to find what was in the literature in addition to whatever was given.
Q. Are you aware that 3M is doing a pilot study in the U.K.?
A. I'd heard that in one of the depositions but I don't remember -- I don't know any details, nothing.
Q. All right.
MR. ASSAAD: Let's take a break for the court reporter.
THE REPORTER: Thank you.
(Recess taken from 11:29 to 11:43 a.m.)
BY MR. ASSAAD:
Q. I just want to go back with respect to Exhibit Number 5. That was attached to your report in Walton. You don't disagree with that; correct?
A. I don't remember it actually, I'm sorry to say.
Q. So you did a lot of work on Walton; correct?
A. I did. I tried to look at that carefully --
Q. Okay.

A. -- and I just can't remember that.
Q. And in fact you -- you know, a lot of the work you did in Walton, except for, you know, stuff dealing directly with Walton with the medical records, you used in your report -- or you had that information that you used in your report in this case; correct?
A. I'm sure there are parts in both, yeah.
Q. Okay. I mean, you didn't start from scratch in this case.
A. No.
Q. Okay. Do you know how much you billed in Walton?
A. Total?
Q. Yes.
A. I don't remember. I don't -- Maybe somebody here has it, but.
Q. Well by the way, when did you -- when did you retire from Virginia Commonwealth University?
A. So, formally 2013.
Q. 2013. So you were retired by the time you started the Walton case; correct?
A. Well, you know, if you were to ask me why'd you do that, it was -- a lot of it was timing, you know, I've always been interested in taking care of these patients. I've never done really a lot

medical/legal.
Q. Well that really wasn't my question.
My question was you were retired by the time you started the Walton case.
A. Yeah, that's right.
Q. Okay.
A. Right about that time, yeah.
Q. Okay. And so after you retired was -- was your -- was most of your income based on doing the Walton case?
A. No. I was fine without it, and the motive wasn't income, because I've never really done much of this. It was just curiosity and timing.
Q. So what were your sources of income after you retired?
A. Oh, I have a very good retirement from TIAA-CREF.
Q. I understand you have a retirement plan, but my question is: Besides your retirement plan, what other income did you -- do you have besides --
A. Besides retirement?
Q. Uh-huh.
A. Occasionally giving talks, sometimes -- yeah, I guess Social Security, if that's what you're asking, as well.

Q. Would you agree with me that most of your income that you've received since 2013 was -- was most likely from working on the Bair Hugger case?
A. No, I would disagree with that. I would guess somewhere a quarter to a third maybe in the last couple years --
Q. Okay.
A. -- of the total.
Q. Now I'm not talking about your pension income. I'm talking about non-pension income.
A. Oh, of non-pension income, yeah. This -- This is a large portion of that.
Q. What percentage?
A. Oh, it's probably, you know, except for -- It's huge. It's probably 80 percent or more, yeah.
Q. Okay. Can you give me roughly how much you -- you billed in Walton?
A. I'm guessing 90,000, something like that, but --
Q. Okay.
A. -- don't hold me to it. Go ask them.
Q. Around that, give or take 10,000?
A. Go ask them. Yeah.
Q. Do you have those invoices still?
A. I don't think so, but they do, I think, so

you --
Q. Greenberg Traurig?
A. Yeah. I would just -- If you need that.
Q. Did you bill any time for Johnson?
A. Probably, yeah.
Q. Do you know how much you billed for Johnson?
A. No. I think -- I lumped them together when I --
Q. Okay.
A. -- gave you that figure, so -- and I'm not trying to be cagey, I just don't remember.
Q. So basically since two thousand -- since you began in -- began working on this case --
A. Yeah.
Q. -- you approximate over $300,000.
A. Yeah.
Q. And my understanding is you -- you billed over $300,000 to do a -- a literature review and to formulate opinions off the literature.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, to -- Yeah. I mean basically I reviewed the literature, came up with opinions, did my best to cite all the articles, pro or con.
Q. Okay. So the answer to my question is

"correct."
A. Yeah. Yeah.
Q. Okay.
A. Well I just made sure that we're -- we're on the same wavelength.
Q. Okay. Did you --
Did you keep an accurate -- accurate time of -- of what you did in this case?
A. Yeah. I have the actual hours by month --
Q. Okay.
A. -- and by day.
Q. Are they underestimated hours, or did you work on --
A. Oh, no. I -- When I sit down, you know, if it's 12:15 I put 12:15. If I get up for a break at 1, I put 1.
Q. Okay. And you also had an assistant that worked on this case; correct?
A. Yes.
Q. Ms. Briley?
A. Yes.
Q. And who is she?
A. She's been my assistant for a long time, and I don't pay her a salary any more, so she helps me do the legal things that I need done, you know, getting

the manuscripts, writing various drafts of the paper, planning any kind of travel that I might have to do related to the case.
Q. Is she a -- like a secretary?
A. Yeah, sort of, but a -- more of a senior administrative type secretary, yeah.
Q. Does she do any research for you?
A. No.
Q. Okay.
(Discussion off the stenographic record.)
(Wenzel Exhibits 6 - 7 marked for identification.)
BY MR. ASSAAD:
Q. What's been marked as Exhibit Number 6 and Number 7 are invoices provided to the plaintiff in this case from you. Does that look like your invoices?
A. Yes.
Q. Okay. And these are invoices that you provided to 3M in working on this case; correct? Or their attorneys?
A. I provided them to the legal firm.
Q. When I say "3M," I'm referring to 3M or their attorneys.
A. Okay.

Q. So it seems that your first invoice on Exhibit Number 6 is dated December 7th, 2015; correct?
A. So I have the righ -- Oh, 6. I'm sorry. So where -- What page are you on?
Q. Look on the first page of 6, it's December 7th, 2015. Or that's invoice for Ms. Briley.
A. That's for -- That's for Barbara Briley, yeah.
Q. Okay. Well if you look on I guess your first invoice, which is dated June 6, 2016 on Exhibit 6?
A. Yeah. Let me go through it. I don't know where we are. Oh.
How many pages in are you?
Q. About six.
A. Okay.
Q. Okay. And that's your invoice is for each month from December 2015 to May 2016; correct?
A. Should be, yeah.
Q. Okay. So basically the first invoice provided to defendants in this -- or to the plaintiffs in this case that we have is for December of 2015; correct?
A. Yeah. Looks like that's the first one there.

Q. But there are invoices that you've worked on a Bair Hugger case prior to December 2015.
A. You're talking about the earlier cases?
Q. Walton and Johnson.
A. Yeah, that's right.
Q. Okay. And based on my calculations, the invoices that were provided to us from you total about $213,000. Does that sound about right?
A. That's about right, I think. I don't know exactly, but it sounds right.
Q. And for Ms. Briley it was $6,860. That sound about right?
A. I don't know. I didn't add up hers, but.
Q. Okay. But you're not going to disagree with the invoices; correct?
A. No.
Q. Does she --
Does she keep all the money that she charges for?
A. Yeah. It all -- It goes directly to her.
Q. Okay.
A. I tried to keep that separate.
Q. And this money goes directly to you, it doesn't go to Virginia Commonwealth University; correct?

A. That's true.
Q. Okay. Do you have a company that it goes to, or it just goes to you personally?
A. No.
Q. Okay.
A. I haven't become sophisticated like that.
Q. And it seems like you spent -- the total number of hours spent is 380 hours -- 380.75 hours. That sound about right?
A. Probably right.
Q. Okay. And Ms. Briley spent about 196 hours; correct?
A. Well I didn't add that up, so I'm assuming you're right.
Q. Okay.
A. If it matches this, you know.
Q. Okay. So that's the total of, you know, over 500 hours between you and Ms. Briley.
A. Umm-hmm.
Q. Is that correct?
A. Yeah.
Q. Okay. And approximately how many hours did you spend on the Walton-Johnson case?
A. I don't know. I mean, that's why I said the total might have been close to $90,000, so.

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Q. And you charge how much per hour?
A. Six hundred.
Q. So 90,000 divided by 600 equals about 150 hours. This sound about right, give or take?
A. That sounds about right.
Q. Okay. So so far between you and M -- Did Ms. Briley work on the Walton case?
A. I think she did, yes.
Q. Do you know how many hours that she billed?
A. I don't, actually. Don't remember that.
Q. So between you and Ms. Briley, and not counting her time on Walton, the two of you spent over 720 hours on this case.
A. Yeah. Sounds about right.
Q. Okay. Did you ever recommend to 3M to -- let's -- to do a study?
A. No.
Q. Okay. Why not?
A. I haven't met with 3M.
Q. Or their attorneys.
A. Ask the attorneys to do a study?
Q. I mean, hey, why don't you recommend -- you should recommend to 3M to do a study?
A. I have never asked them that.
Q. Okay. You're not an expert in aerobiology;

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correct?
A. I'm not an expert in aerobiology.
Q. You're not an expert in microbiology; correct?
A. In what?
Q. Microbiology?
A. Well, I'd caution you there. I mean, I think microbiology is the basis of infectious diseases, and in that interface between micro and infectious disease I am an expert.
Q. But you're not an microbiologist.
A. I'm not a -- I don't have a degree in microbiology.
Q. Okay. You don't consider yourself an expert in orthopedics; correct?
A. Only the interface, again, between orthopedics and infectious diseases. I'm not an orthopedic surgeon.
Q. You don't consider yourself an expert in medical device design; correct?
A. That's true.
Q. You don't consider yourself an expert in medical device warnings; correct?
A. Warnings, no.
Q. You don't consider yourself an expert in

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patient warming; correct?
A. In what?
Q. Patient warming.
A. A expert in patient warming?
Q. Yeah.
A. Only as it is influenced in this case with the infectious disease part, but not --
Q. And everything that you opine is going to be --
A. -- warming.
Q. -- is going to be based on a literature review and not your own personal --
A. That's true.
Q. -- directed research.
A. Yes, that's --
(Interruption by the reporter.)
(Discussion off the stenographic record.)
Q. Correct?
A. Yes.
Q. Okay. You're not an expert in operating room design; correct?
A. Correct.
Q. Have you read any of the ASHRAE articles or chapters regarding operating room design?

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A. Don't think so.
Q. Are you aware that it is estimated between one million to 900 million skin squames are shed during a two- to four-hour surgery?
MR. COREY GORDON: Object to the form of the question.
A. So I didn't go to the primary literature but I've seen that in a couple depositions.
Q. Do you disagree with that?
A. No reason to disagree or agree.
Q. Okay. You have no experience in operating-room airflow; correct?
A. Any experience, no.
Q. Okay. You don't consider you're an expert in operating airflow?
A. That's true.
Q. I think I've asked you this before, but you're not an expert in particle flow; correct?
A. In particle flow, no. I'm not.
Q. Do you agree with me that Dr. Elghobashi is an expert in particle flow and turbulent air?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. I have no idea of his expertise.
Q. Well you've rea -- you've seen his report;

correct?
A. Yeah. I didn't understand most of it.
Q. Did you --
And you didn't have an opportunity to compare our expert's report to defense expert's report; did you?
A. No. Only what I saw on Science Day, basically.
Q. Okay. And you're not an expert in turbulent flow; correct?
A. In turbulent flow? No, I'm not an expert in turbulent flow.
Q. Okay. Have you read the Complaint in this case?
A. I think I may have read it at the time of Walton, and -- I remember seeing that.
Q. Okay.
A. More recently I don't think I looked at anything.
Q. What is your understanding of plaintiffs' claims in this case with respect to the mechanism of injury of a Bair Hugger causing a -- an infection?
A. My understanding is that the plaintiffs are saying that there is heat generated from the Bair Hugger, and it creates currents, particularly --

including, at least, a downflow current towards the floor, whipping up some kind of particles into the air near the operative site, and therefore they think that the Bair Hugger, having done that, relates to infections. That's my understanding.
Q. You don't disagree that the Bair Hugger generates heat; correct?
A. It does generate some heat.
Q. Well do you know how much heat?
A. I don't.
Q. Okay. Well you used the term "some." Do you know -- You're just -- you're not --
You're not quantifying it; correct?
A. I'm not.
Q. Okay. You do agree that the Bair Hugger, the holes are facing down; correct?
A. Yes.
Q. Onto the patient?
A. Yes.
Q. In an orthopedic surgery.
A. Yes.
Q. Okay. So you do agree that it creates current, air currents.
A. I think it does.
Q. Okay. And you agree that --

Do you know what the first law of thermodynamics is?
A. No. I know you like to ask that question, but I don't know it.
Q. How do you know I like to ask that question?
A. Somewhere in -- you were deposing somebody and it was one of your earlier questions.
Q. Okay. Do you agree that hot air is less dense than cold air? If you know.
A. Yes, I think. Less dense, yes.
Q. You've seen a hot air balloon; correct?
A. Yes.
Q. Okay. And hot air balloons actually rise; correct?
A. Yeah, they do.
Q. Okay. You're not going to disagree with the laws of thermodynamics; are you?
A. I have no idea what the law of thermodynamics is.
Q. Okay. Okay. You're going to defer to the engineers in this case.
A. To you.
Q. To me? You'd defer --
A. Yeah.
Q. -- to me as well. Okay.

Unfortunately, I can't testify.
(Laughter.)
Q. Which is a good thing, because I think Corey would love to take my deposition.
And you agree with me that skin squames have a mass; correct?
A. "Have a mass"? You mean they're not just energy, is that what you're asking?
Q. Yes.
A. Yes.
Q. Okay. And you agree with me that gravity exists in an operating room; correct?
A. It exists everywhere.
Q. Okay. Now just so I understand your opinion, assuming that the plaintiffs' engineering theory is correct that the hot air causes contaminated air from underneath the operating table to rise to above the operating room surgical table, is it correct that your opinion is going to be that since you believe that most of the surgical-site infections are caused by the patient's flora, that the effect of the Bair Hugger is irrelevant?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.
A. I've told you separately I think most

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infections come from the patient flora, no question. Now you're asking me a hypothetical assuming that everything that the plaintiffs say is correct, would that have an influence. And it might, but that's an assumption.

Q. So -- So if the plaintiffs are correct that the Bair Hugger causes contaminants from underneath the operating room floor to actually go into the -- above and into the surgical site, that may have an effect on your opinion?

A. If everything that you say was validated, and I don't -- I don't think we're there yet, in this hypothetical situation, it might contribute. We have no data, I think, to really convince people that the Bair Hugger actually leads to infections.

Q. Okay. How do we get there?

A. How do we get the data?

Q. Yeah.

A. Well what I've tried to do is do the following.

Q. Well I understand what you did. You said we're not there yet. That was your -- That was your answer. So how do we -- What would you do today to determine the answer to that question? Not looking at literature in the past, but what would you do today?

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A. So if -- if there, you know, was a study that was being planned, one of the things I would do is link the -- what was found in the air, microbiologically, with what was found somewhere else, not on the patient flora, if you could do that. Because you're positing that things come up from the floor. And link what's on the floor, link what's in the air and link what's in the patient's wound, and show me it's the same -- pick a organism, Staph aureus, with the same fingerprint.

Q. Okay. And how many patients do you think you would need to do that study?

A. I don't know.

Q. Like -- Like 50, a thousand, 10,000?

MR. COREY GORDON: Object to the form of the question, lack of foundation.

A. Well --

Q. And I'm talking about with respect to a total hip or total knee arthroplasty.

A. You'd need a lot of patients to show -- to show that. And you have to do a multi-centered study, and we'll get a statistician to look at what you'd expect. But I, off the cuff, wouldn't come up with an answer.

Q. So you'd want to do microbiological sampling

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of, like, what's underneath the operating room table; correct?

A. Yeah, because you said that's where it starts.

Q. And you want to do microbio -- microbiological sampling of the patient's flora in the wound.

A. Right.

Q. Okay. And I think you said one other microbiologic sample.

A. It would have to be in the air --

Q. Okay.

A. -- because you said it comes up in the air, in your hypothetical.

Q. So what's in the air before you turn the Bair Hugger on; correct?

A. Before and during.

Q. Okay, during.

And then you want to also determine which patients obtained infections; correct?

A. Right. Right.

Q. And so for total hip and total knee you might need 10,000 patients.

A. A lot of patients.

Q. Okay. And so that study would be very,

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very, very expensive; correct?

A. Ten thousand patient would be expensive.

Q. Okay. And to do all that microbiological sampling would be expensive too.

A. Right. Truth is costly sometimes.

Q. Okay. And -- And you agree with me, based on your experience of doing research, that probably the only person that would ever fund a study such like that or -- would be the manufacturer of the device.

MR. COREY GORDON: Object to the form of the question.

A. I'm not sure if NI -- it'd take awhile to get NIH involved in that, but at least I'd give it a try if I were really going to go into that.

Q. But the NIH, you know --

A. But typically they don't --

Q. -- funds very little studies.

A. Typically they don't get into devices and --

But the mechanism might be important as a general surgery issue. Forget just hips and, you know, prostheses.

So if you could expand it, I wouldn't be surprised that, you know, a well written, general surgery person could maybe convince them to do -- to look at it.

Q. When you say "the mechanism," what do you mean by "the mechanism"?
A. In other words, if the question is what's the pathogenesis of surgical-site infections, that's what I would be asking in the front end. And if you said it's not just that we're going to look at hips and knees, because the numbers might be very high, but let's look at some general surgery patients.
The reason, for example, that Kurz and Melling looked at the patients they did, particularly Kurz, because of the high infection rate with colorectal surgery.
Q. But colorectal is a -- is a -- is considered a dirty surgery; correct?
A. It is. It's clean contaminated.
Q. Clea -- Okay. Well there's clean, there's clean contaminated, and then there is --
What's the third one?
A. Contaminated where you've cut across a tube, essentially. So in other words, gallbladder duct, something like that.
Q. So cutting into the -- the colorectal area is not considered contaminated?
A. I think it depends on how much spillage there is.

Q. Okay.
A. And then contaminated obviously if there's already --
Q. Okay.
A. -- an infection.
Q. So you want to look at the mechanism of injury with respec -- look at the mechanisms across the board; correct? Is that what I'm understanding?
A. No. If you were going to design a study, you know, my label would be what's the pathogenesis of surgical-site infections. And I think, you know, so far what I've learned is that it's the patient's microbiome that's the source.
Now what I think you're getting at is a very interesting question. What's -- How does it get from the source to the wound? And you're positing, in your hypothetical, that maybe it's not the patient's microbiome but it's something on the base of the floor being wafted up. So I would like to try to put that to rest one way or another.
That make sense? I'm trying to...
Q. You agree that implant surgeries are more susceptible to infection than non-implant surgeries.
A. Well let's pause for a second. I'm not sure the pathogenesis of the initiation is different, but

once the infection is present, once you have the biofilm, then it's -- it's much harder to cure and almost always you have to then replace the -- the joint because the foreign body is going to hold the organisms there.
But if you said what's the initiation phase I think you still start with the flora, patient flora. And I think the patient's flora is there at the time of surgery, at the time of the incision. That's my current thinking.
Q. Okay.
A. And then once the infection -- because I know that you've discussed with other people, you know, biofilm. That's a different story. Once you have that, the therapy and then the -- the late pathogenesis, there's no question, if that's what you're asking, is different in a device-related infection than a non-device-related infection.
Q. So is it your opinion that the infection dose for a implant infection is the same for a superficial wound infection? Is the infection dose --
A. You know we know so little about infectious dose, but I think the initiation might be -- I don't know. I don't know how to answer that question for sure.

Q. Well if you don't know you can say you don't know.
A. Yeah. So I don't know, --
Q. All right.
A. -- there aren't...
Q. That's fine.
A. But I thought we were talking hypotheticals, and that's --
Q. Well you mentioned -- you discussed the rabbit studies and the mice studies; correct?
A. Yeah. Right.
Q. And many of those studies, and we can go through them if you want, but let's try to get here --
A. Yeah. No. That's --
Q. -- out of here by six o'clock.
A. Yeah. No. That's fine. Yeah.
Q. Most of those studies indicated that when there is an implant the infectious dose is much less than when there's no implant.
A. I think in general that's true.
Q. Okay.
A. There's probably less based on the animal studies, yeah.
Q. And in fact if you looked at the rabbit study, and let's go to --

A. I'm thinking you're probably looking for the end of the...
Q. Yeah, you're right.
(Interruption by the reporter.)
A. The end of the report.
Q. Okay. Page 77.
A. Yeah.
Q. Okay. So --
And you've looked at these studies; correct?
A. I have. That's where I made the table from, and...
Q. Okay.
A. And this doesn't -- I don't mean to imply it's a comprehensive look, but it's a sample.
And what I come away with is the infecting dose varies by which animal and which mechanism that you're infecting the animal.
Q. But in the Southwood study of 1985, when a medullary inoculation with prosthesis, which means they actually kept the prosthesis in; correct?
A. Right.
Q. Okay. The other ones they did not keep the prosthesis in; correct? The other three --
They had four different routes of infection; correct?

A. I didn't count them all, but they're -- you know, they're -- they're numerous, yeah.
Q. Okay.
A. This was the intravenous study. Is that the one you're referring to?
Q. Yeah. Hold on one second, just pulling it up so that we're on the same page.
They had four groups; correct?
A. I don't remember exactly, but.
Q. You have route of infection number IV here at -- near the top; correct?
A. Okay. All right.
Q. And --
A. Oh, I see what you're saying. These four, yeah.
Q. And --
(Discussion off the stenographic record.)
MR. COREY GORDON: Is that roman numeral, or is that intravenous?
THE WITNESS: Oh, that's -- No, it's "I-V," intravenous.
MR. ASSAAD: Oh, it's "I-V"? Okay.
THE WITNESS: Yeah. That's why I thought you meant the studies here.
BY MR. ASSAAD:

Q. The reason why I ask is they also have groups I, II, III, IV in Roman numerals.
THE WITNESS: I'm glad you said something there [to counsel].
(Discussion off the stenographic record.)
(Wenzel Exhibit 8 marked for identification.)
BY MR. ASSAAD:
Q. Doctor, Exhibit Number 8 is the -- is the Southwood article referred on page 77 of your report of Exhibit 1; correct?
A. Yes.
Q. Okay. Let's look at --
Let's explain to the ladies and gentlemen of the jury what ID50 means.
A. It's the dose of organism that will infect 50 percent of the subjects --
Q. Okay.
A. -- as opposed to the dose, you know, which required to infect 10 percent or a hundred percent.
Q. And a dose would be considered a CFU?
A. In this case, yes.
Q. Okay. So in this case it would be a CFU; correct?
A. Yes.

Q. Let's turn to Figure 2 on page 230 of Exhibit 8. It's the second page.
A. Table 2, or Figure 2?
Q. Or Figure 2. I'm sorry.
And they talk about four different types of ways they infected the rabbit; correct?
A. Yeah. I'm trying to remember the study. Yeah.
Q. One was --
The first one was medullary, they infected the actual implant; correct?
A. Yes.
Q. Then they did medullary but they took out the prosthesis; correct?
A. Yes.
Q. And then they did a delayed intravenous and an intravenous; correct?
A. Yeah.
Q. Okay. And let's look down at the calculations they did, and it says: "In Group I (medullary peroperative inoculation) ID50 equals 1 .3 times 10 to the 1.114"; correct?
A. Where are we?
Q. The description of Figure 2. The small writing right below the figures.

A. Oh, I see. Okay. The range of inocula? Yeah. (Witness reviewing exhibit.)
Q. Okay. That means how much bacteria -- what's the effective dose for 50 percent when you -- you add back -- add CFUs to the implant; correct?
A. Yeah.
Q. Okay. Have you calculated what 1.3 times 10 to the 1.114 is?
A. No. It's low. It's a small number.
Q. Uh-huh. I'm going to calculate it for you, let me see if you agree with me.
A. It's probably 15 or 20.
Q. 1.3 times 10 to the 1.114. [Calculating.] About 17; correct?
A. I was pretty close.
Q. Okay. Or, I'm sorry, 1.7. Is it 1.7? I'm sorry. Let me calculate it again. [Calculating.] It's below 20; correct? Whatever it is, it is; correct?
A. It's low.
Q. That's a very low number; correct?
A. Yeah.
Q. Okay. Compared to the in -- the infection dose for groups II, III and IV, which are 10 to the 5; correct?

A. Yeah.
Q. Okay. Which are very large numbers; correct?
A. They're big numbers. Bigger than 10 to the --
Q. So you agree with me then when -- at least in the rabbit case, that when -- the infective dose when a bacteria gets on the implant is much lower than when it's not on the implant.
A. That's what the study showed.
Q. And do you disagree with that study?
A. No.
Q. Okay. And in fact you agree with me that one skin squame can carry, you know, multiple CFUs.
A. I think I've read that, that they can car -- can carry, sometimes, several, up to three or four or something.
Q. Even more.
MR. COREY GORDON: Object to the form of the question.
Q. I mean, you agree with me that there is 10 times more bacteria on our skin than actual skin cells.
A. Than actual what?
Q. Than our skin cells.

A. Well it's not just skin, the -- what I cited was the total flora on the body.
Q. I understand. But the total flora, there's 10 times more flora on our skin than actual skin cells.
A. Yeah.
Q. Okay. And the flora is bacteria; correct?
A. When you say flora, it's bacteria, it's fungus --
Q. Okay.
A. -- some parts of the body it's virus.
Q. Okay. So in fact you could say that for every skin cell there's -- there's 10 flora, on average.
A. So for every skin cell there are 10 -- Yeah.
Q. Okay.
A. There might be more bacteria, yeah.
Q. So in fact a skin squame could carry more than three or four bacteria.
A. Okay. I haven't looked at that recently, but yeah.
Q. But the math -- the math makes sense; correct?
A. Okay.
Q. Do you agree?

A. I think I've seen up to --
Q. Okay.
A. -- four or five.
Q. Okay. And some might have a cluster on it that might have 20, 30.
A. Yeah, I don't know that.
Q. Okay. I mean, bacteria go into clusters; correct?
A. They do clump.
Q. Okay. And they could clump as few as 3 and as many as hundreds.
A. Yeah, I don't know about hundreds. I just -- I just can't say I know that, but maybe.
Q. More than ten.
A. Yeah.
Q. Probably more than twenty.
A. I don't know.
Q. Okay. So there is a difference with respect to the infection dose of an implant if the bacteria lands on an implant as compared to the -- if the bacteria lands on -- on skin.
A. That's not what they really showed. They didn't say "land on." They injected it.
Q. Okay. Well --
A. That's different. Surgeons don't go in and

shoot a number of organisms into the joint.
Q. Well you agree with me that -- forget about the way it -- the bacteria gets there, okay, whether or not it's -- it's injected. I mean, the bacteria got to the joint in this case; correct? To the -- the prosthesis.
A. But how can I forget how they got there?
Q. Okay.
A. I'm not sure --
Q. So is that a limitation of the study?
A. Oh. Well if you want to posit that the air is important, nobody has done the infectious dose by the air.
Q. Well that would be unethical, wouldn't it, in a human?
A. Well that would be unethical in a human, but you could count, in the study that I was proposing, or in another study, show me that one organism in the air, a markered orga -- markered species that landed later into the wound, not start with the wound and go out, --
Q. Let me ask you this --
A. -- and then caused an infection with that same --
Q. Okay.

A. -- genus and species and same fingerprint.
Q. Let me ask you this question.
A. Yeah.
Q. If Darouiche's study, the one that came out recently which you emailed him about. Do you recall that?
A. Yeah.
Q. Okay. He did a microbiology study and it indicated that the -- the -- the bacteria came from the air, you know, because of the increased bacterial load over -- over the surgical site. Would that change your opinion in this case?
A. What he showed was a correlation between particles and bacteria and the four infections, and he modeled that to get the correlation.
Q. And your criticism of him is that he didn't do any microbiological testing.
A. That's one, yeah, sure. I think that's important.
Q. Because you're not sure whether the bacteria came from the flora or from the air; correct? The patient's flora or the air.
A. Yeah.
Q. Okay. If he did do microbiological testing and indicated that the bacteria that caused the

infections came from the bacteria that was in the air, would that change your opinion with respect to whether or not bacterial load in the air has a -- has a impact on periprosthetic joint infections?
A. Well --
MR. COREY GORDON: Object to the form of the question, --
A. Yeah.
MR. COREY GORDON: -- misstate -- mischaracterizes his testimony.
THE WITNESS: Thank you. I didn't mean to interrupt, but.
A. So one of the things you would like to know is if there's an organism in the air and if we did this hypothetical study where we actually had good microbiology; did it start, first of all, in the flora of the patient, the microbiome, somehow get into the air -- I mean, I can imagine how that might happen, and then land -- or are we talking about a totally different organism that started on the ground, which is what you postulated initially, got whipped up by a device and then hung over the wound and then caused the infection.
Q. Are you asking me a question?
A. Well, no. I'm just trying to answer you.

Q. Well let's see -- let's go to the Darouiche article just a couple things.
A. Okay.
Q. You do understand that he found a correlation between bacterial load in the air and periprosthetic joint infections, but no correlation with superficial wound infections.
A. That's what he said, yeah.
Q. Do you agree with that?
A. Yeah. No, he said that.
Q. Okay. But do you have any disagreement of that, --
MR. COREY GORDON: Object to the form of the question.
Q. -- or criticism of that?
A. He's reporting what he found, and I'm saying if that's what he reported, that's what we'll go with.
Q. Well, doctor, you've done a huge literature review and you've agreed with some articles, you've disagreed with some articles. I'm asking: Do you disagree with that conclusion?
A. On his? No.
Q. Okay.
A. I mean, that's what he found.
Q. Okay. And you don't disagree with it.

A. Yeah.
Q. Okay. So you agree that the bacterial sampling over the surgical site in the Darouiche study has a direct correlation with periprosthetic joint infection, you just don't know where that bacteria came from. Is that correct?
MR. COREY GORDON: Object to the form of the question.
A. I surely don't know where the bacteria came from, and he certainly didn't match it to his four infections. It's a very small number of infections, but he didn't match it.
Q. But we do know that when the bacterial load, the CFUs were increased over the -- over the surgical site that there was a statistically significant increase in periprosthetic joint infections; correct?
A. That was his correlation, absolutely correct.
Q. And you don't disagree with that.
A. No.
Q. Okay. Your -- Your criticism is you don't know whether that bacteria came from the patient's flora or from somewhere else, and there needs to be further testing to determine that.
A. Has to be a lot more testing to know whether

or not any of those bacteria he found were involved in the infections.
Q. Okay. So we need to do microbiological testing. That's your criticism.
A. Absolutely.
Q. Okay.
A. And, you know --
Q. Okay.
A. -- what -- what, three Staph and one mixed infection.
(Discussion off the stenographic record.)
MR. ASSAAD: Let's take a break for lunch, guys.
THE WITNESS: Okay.
THE REPORTER: Off the record, please.
(Luncheon recess taken at approximately 12:23 p.m.)

AFTERNOON SESSION
(Deposition reconvened at approximately 12:53 p.m.)
BY MR. ASSAAD:
Q. Are you ready to continue, doctor?
A. Sure. Thank you.
Q. Let's go to page 77 of your report regarding the animal studies.
A. Okay.
Q. And you cited these studies because you believe they help you formulate your opinion; correct?
A. Yes.
Q. And you believe that they're authoritative; correct?
A. Yes.
Q. Okay. Let's go to the New Zealand study of white rabbits?
MR. COREY GORDON: Exhibit 8?
A. Oh, Craig? Okay.
MR. COREY GORDON: Oh. I'm sorry.
Q. And that's a -- They used 10 animals, and they inoculated the -- the rabbits with 10 times 5 to 10 times 8 CFUs; correct?
A. Yeah, I have 10 to the 2, 10 to the 4. Maybe I missed that somewhere.

Q. The third one down, New Zealand --
A. Oh, third one down.
Q. Yes.
A. Oh, okay.
Q. I'm sorry, that's the second New Zealand.
A. All right. Okay.
Q. New Zealand likes their rabbits, I guess, huh?
A. Yeah. Okay. Got it.
Q. So you agree that study wasn't -- it was just to show the mechanism of these implants getting infected, they didn't look at inoculation dose.
A. Well a lot of studies in fact are trying to get as high a infected dose so they can actually track what's going on with these type of infections rather than scaling up the dose to know exactly what the ID50 is, for example.
Q. Exactly.
And this study, if you recall, they were looking about ho -- tracking the infection and they did MRIs and everything. Do you recall?
A. Umm-hmm.
Q. "Yes"?
A. Yes.
Q. Okay.

(Discussion off the stenographic record.)
(Wenzel Exhibit 9 marked for identification.)
(Discussion off the stenographic record.)
BY MR. ASSAAD:
Q. Doctor, you've read this study; correct?
A. I have.
Q. And you relied upon this study; correct?
A. I did.
Q. Okay. Let's go to the "Discussion" section on page 3 of this study.
A. Okay.
Q. On the second paragraph under "Discussion" it says: "Because the main source of contamination in total joint replacement is wound infection via operating room air, we attempted to mimic perioperative contamination by inoculating the bacteria into the joint immediately after wound closure."
Did I read that correctly?
A. Yes. That's what they say.
Q. You disagree with that; don't you?
A. I do.
Q. Okay. So disagree with a study that you think is authoritative; correct?

A. Well the focus I had was on the infecting dose.
Q. Okay.
A. That's what I was trying to get at.
Q. Well this didn't really talk about infecting dose, this was more of, like, what occurs when the patien -- when the -- when the rabbit gets infected, and following the infection by doing MRI; correct?
MR. COREY GORDON: Object to the form of the question.
A. What --
Q. Correct; "yes" or "no"?
A. In other words, I'm trying to find any data that I could, at least in a brief survey, of what it takes to infect the joint, --
Q. Okay. So you like --
A. -- and this was one of the studies.
Q. So you like to take -- you like to take the data that supports your position --
A. No.
Q. -- and then disregard data that doesn't support your position; correct?
A. No, that's not true.
Q. So you think that --
A. I've already shown you studies where there

were data that I had, some clinical data, where it didn't support it, so you know that.
Q. But you disregard the -- the -- these authors here that did this study that said that the -- that -- that the main source of contamination in total joint replacement is wound infection via operating room.
You disregard that; correct?
A. I disagree with that. That had nothing related -- They didn't look at where the organisms came from here. They had them in the syringe and injected them.
Q. Okay. But that's why they injected them the way they did; correct?
MR. COREY GORDON: Object to the form of the question, also lack of foundation.
Q. I mean --
A. I don't know why they did what they did, but they do say that they -- they think it's airborne. I disagree with that.
Q. It says --
A. They injected animals, and that's the kind of dose that they used to get infection.
Q. "...we attempted to mimic perioperative contamination by inoculating the bacteria in the joint

immediately after wound closure."
Did I read that correctly?
A. Yes.
Q. And they did that because the main source of contamination, according to them, in total re -- joint replacement is wound infection via operating room air; correct?
A. That's what they said.
MR. COREY GORDON: Object to the form of the question, lack of foundation.
Q. Going to page 78.
A. Okay.
Q. Under the sheep model, --
A. Yeah.
Q. -- Williams D. L., --
A. Yeah.
Q. -- the Journal of Biomedical Materials; correct?
A. Yes.
Q. They inoculated the sheep with only 10 CFU; correct?
A. Yeah, on the membrane.
Q. Okay. And that's not that many CFU; correct?
A. That's a low number.

Q. Okay. And in fact isn't it fair or accurate that in this point in time you have absolutely no opinion to the amount of CFUs required to cause a periprosthetic joint infection?
A. What I would say is that I think -- I think it's fewer organisms to cause a periprosthetic infection than with a non-periprosthetic infection. If you asked me to come up with a number, it's harder to find that. You want me to pick a number and?
Q. I don't want you to guess.
A. Yeah.
Q. I mean, I'm looking at your last paragraph.
A. Yeah.
Q. I mean, you do say, "It is generally thought that with a foreign body (joint prosthesis), the infecting dose of bacteria is less than that for surgeries in which no foreign device is placed"; correct?
A. And I stand by that.
Q. Okay. You just don't know what the infecting dose is; correct?
A. That's true.
Q. But we could agree, based on some of the rabbit models, that it could be as low as 17.
A. No, that's not true. In the experimental

model, yes, you can create an infection by injecting organisms directly into the joint or injecting organisms into the vein. That's not what surgeons do when they're putting a prosthesis in. They don't take a syringe of Staph, inject it directly into the joint or put it into the IV.
Q. Can we agree at least that it's at least a magnitude of 100 times less between a superficial and a prosthetic?
A. I don't know -- I don't know what the number is, so I've told you that. I think it's going to be less. I don't know.
Q. How much less?
A. I don't know.
You asked me to, you know, come up with a number, and then you say, well don't guess, because there just aren't the data.
Now the other thing to tell you related to -- You want to jump from here to people, which is fine --
Q. I don't want to jump to people yet.
A. -- you know, but, you know, to infect a rabbit by injecting it into the joint, I would say, yes, it takes very few bacteria.
Q. Okay.

A. That's what I'll know from this study. Or sheep, in this case.
Q. And as little --
When you're injecting as little as 17 bacteria.
A. They're very low numbers, yeah.
Q. But the rabbit study we showed 17 --
A. Yeah.
Q. -- bacteria based on the IV -- for 50 percent of the population from rabbits; --
A. Yeah.
Q. -- correct?
A. I think that's right.
Where was that where you're referring to?
Q. On the first one, the Southwood.
A. The Southwood. Okay.
Yeah.
Q. Okay?
A. Yeah.
Q. And that's for 50 percent of the population to infect; correct?
A. Of animals, right.
Q. Okay. So that means 17 CFUs would infect 50 percent of the rabbits in that scenario.
A. If you inject them.

Q. If you inject them.
Which means that there is a percentage of people that -- percentage of rabbits that require less than --
A. Might be.
Q. -- 17 CFU --
A. Might be.
Q. -- to cause an infection.
A. Yeah.
Q. Okay.
(Interruption by the reporter.)
BY MR. ASSAAD:
Q. And in fact if you go back to Exhibit Number 8, you see that under Figure 2 that as little as one CFU could cause an infection in the rabbits under the medullary graph.
A. 1.3 times 10 to the something.
Q. No. I'm looking at the graph itself. You see where -- You see where it says "Medullary (no prosthesis)", it starts around 20?
A. Yeah.
Q. Okay. That means for anything below 20 times 10 to the X there was no infection; correct?
A. Yes.
Q. But with the medullary where there was a

prosthesis you agree that it almost starts at zero.
A. It's very low.
Q. Very low. Less than 17.
A. Yes.
MR. COREY GORDON: Object to the form of the question.
Q. Okay. 17 CFUs was for the 50 percent; correct?
A. That's what they found.
Q. Okay.
(Wenzel Exhibit 10 marked for identification.)
BY MR. ASSAAD:
Q. What's been marked as Exhibit 10 are emails between you and Dr. Darouiche that was provided to us. This look like the email that you've had between him?
A. Yes.
Q. And I just want to talk about one thing. During -- During --
You questioned him about this study in formulating your opinions in this case; correct?
A. Yeah.
Q. Okay. And in fact one of your questions was whether or not a forced-air warming device was used in the operating room during his -- during the study in

which he compared biological load and surgical-site -- and periprosthetic joint infections; correct?
A. Yes.
Q. And you found out that all patients were used -- were given a warming device; correct?
A. That's what he said.
Q. Okay. That's all I have.
What is the difference between a superficial surgical-site infection and a periprosthetic joint infection?
A. Well a deep infection would be that at the fascia level or below.
Q. Is a deep joint infection different than a periprosthetic joint infection?
A. I would classify them the same as deep infection.
Q. Well you could have a deep infection but not have -- but it doesn't reach the joint; correct?
A. Could possibly, yeah.
Q. Okay.
A. But by that time you're in trouble, yeah.
Q. You're in trouble, but there is a distinction; correct?
A. There could be, yeah.
Q. Okay. I mean, there is technically a

superficial surgical-site infection; correct? Which is --
A. There are superficial.
Q. -- pretty much the skin area and the first couple layers, the first --
A. Yeah.
Q. Okay. Then you have a deep joint, which can include the -- or --
So you could have a deep -- a deep infection, right, which could include the joint or may not include the joint; correct?
A. Yes.
Q. And then you have a periprosthetic joint infection which definitely includes the joint; correct?
A. That is the same.
Q. Okay.
A. I would use the same.
Q. You'd use the same?
A. Yeah.
Q. You've never seen it in the literature where it's been distinguished?
A. No, I said I would -- I would say a periprosthetic joint is a deep joint infection, yeah.
Q. Okay. But a deep joint infection may not

include the peripros --
A. May not.
Q. Okay.
(Interruption by the reporter.)
Q. A deep joint infection may not include a periprosthetic joint infection; correct?
A. Yes.
Q. Okay. And in fact you agree with me that you could have a periprosthetic joint infection and not have a superficial surgical-site infection.
A. Yes.
Q. Okay. And in fact you could have a periprosthetic joint infection and not have a -- a deep wound infection.
A. Yeah, I can't cite anything where I know that, yeah.
Q. And you agree that with respect to a periprosthetic joint infection, that the most likely time that a -- a patient obtained the bacteria that causes the periprosthetic joint infection was during the time that the patient was in surgery.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, most people think that's the time when things happen.

Q. You don't disagree with that.
A. No.
Q. Okay. Now let's just assume that we're dealing with a -- a periprosthetic joint infection that is not also a superficial wound infection. You agree that the bacteria that causes the infection occurred perioperatively.
A. Yes, --
MR. COREY GORDON: Object to the form of the question.
A. -- I think so.
Q. As compared to someone having an untreated superficial wound infection that tunneled down to the joint.
A. I see what you're saying, yes.
Q. Okay. So you agree with that; correct?
A. Yeah.
Q. And what is your opinion on what is getting infect -- what -- where the bacteria is -- where the bacteria is when a periprosthetic joint infection -- And let me rephrase. That was a bad question. Strike that.
You agree it's possible that the implant itself could have bacteria on it before it's even placed in the joint.

A. Is it possible that --
Q. Yes.
A. -- that it could happen?
Q. Yes.
A. I can't cite a study but, you know, I never say "always" or "never."
Q. Well, for example, if a person handling the implant prior to placing it into the -- into the joint, if the person's hands are not sterile and has contaminants you might contaminate the implant; correct?
A. So in a hypothetical situation if somebody contaminates the implant, the implant is contaminated.
Q. Yes.
A. Yes.
Q. Okay. And, I mean, with everything, even instruments, we sterilize instruments because we don't want contaminated instruments to cause infection; correct?
A. That's right.
Q. There's been studies that sterilization of instruments reduces the incident of infection; correct?
A. I think so.
Q. I mean, otherwise -- I mean -- I mean,

that's just common knowledge; correct?
A. Yes.
Q. I mean in fact there's really no prospective study that washing hands reduces the incident of infection; is there?
A. I think there's lots of studies that show that.
Q. Prospective or retrospective?
A. Probably I would go back to Semmelweis.
Q. Okay.
(Interruption by the reporter.)
(Discussion off the stenographic record.)
A. Do you understand his studies?
Q. I know the study, but wasn't that retrospective?
A. He was there through the whole time.
(Discussion off the stenographic record.)
Q. But in any event, we agree that if devices that are used during a surgical procedure are contaminated, they may cause infections.
A. If you have a contaminated instrument, it's certainly possible that something might happen and the patient could get infected.
Q. And that -- that would be considered an exogenous source; correct?

A. It would be considered an exogenous source, but let's make sure that we have the terms down. If the -- If the instrument that you are saying in this hypothetical case actually was contaminated with the patient's own flora, then we have to have a little bit more strict definition.
Q. And I understand that. And that's why after usually the first incision they change the scalpel so they don't infect the wound with the patient's flora; correct?
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence.
A. As far as I know that's correct, yeah.
Q. Okay. I mean, you do understand that orthopedic surgeons and the hospital staff in an operating room have -- place procedures and techniques to reduce the risks of infection during an operating procedure.
A. Surgeons hate to have an infection.
Q. Okay.
A. They really never want to have one.
Q. And in fact are you aware that many surgeons, before they touch the implant, change their gloves?
A. Yes.

Q. Okay. Because they don't want to infect the implant; correct?
MR. COREY GORDON: Object to the form of the question.
Q. Because if you -- if bacteria gets on the implant, it may form biofilm and cause a serious periprosthetic joint infection; correct?
MR. COREY GORDON: Same objection.
A. What I would say about biofilm, biofilm is -- occurs after the organisms are onto the implant. So contaminated hands don't cause a biofilm. The organisms land on a site, there is a process under which quorum sensing occurs, and you know what I'm talking about. And with quorum sensing then the biofilm is formed. It's sort of like a broadcast email to the other organisms to start making biofilm.
Q. And I understand that.
My question was that the -- I'm not saying that the surgeon transfers biofilm. Listen to my question.
The surgeon changes his gloves because he doesn't want to contaminate the implant; correct?
A. I think that's correct.
Q. Okay. And the reason why you don't want to cause an im --

And the reason why he changes his gloves is because he doesn't want to place any bacteria on the implant; correct?
A. I think he wants to minimize any possibility.
Q. Okay. And then after the im --
And then the implant is placed, and that bacteria, at a later point in time, may cause biofilm, which would make it very difficult for the body to fight off.
A. In that scenario it could happen.
Q. Okay. And in fact they do all this to not infect the patient; correct?
A. Surgeons hate to have an infection.
Q. And have you yourself looked at an implant under an electron microscope?
A. No.
Q. Okay. Are you aware that an implant is not smooth and there are many crevices for bacteria to place themselves in?
A. Well I haven't looked at one, but it doesn't surprise me, but I haven't looked at one.
Q. Okay. And you understand that the reason why the body has a difficult time removing an infection or bacteria from an implant is because

there's very little vascularity to the implant.
A. It's the --
THE WITNESS: Go ahead. I'm sorry.
MR. COREY GORDON: No. Go ahead.
A. It's the low vascularity and the biofilm I think are a couple of key --
Q. Is there any vascularity to an implant?
A. None.
Q. Okay. So you would agree with me that once someone has an infected implant, giving the patient antibiotics without any type of vascularity is pretty much ineffective.
A. That's not true. There are people in Switzerland that have actually gone to drugs that penetrate the biofilm. Examples of such antibiotics include the fluoroquinolones and rifampin.
(Interruption by the reporter.)
THE WITNESS: Fluoroquinolones. Sorry. Fluoroquinolones and rifampin.
A. And they've been able to spare patients -- and I don't know totally what the follow-up is, so -- but 6 to 12 months later, without having to take the implant out. This is a hot area that people are trying to look at, because it's devastating to have the implant removed.

Q. I understand. And -- And that's in --
And that's in Switzerland, you said?
A. Yeah.
Q. Okay. But in the United States are we using those drugs yet?
A. We are.
Q. Okay. And you don't know how effective they are.
A. They look effective, and so when we're treating these infections, we're -- you know, trying to cool things down if it's already infected, we will often use a drug that penetrates biofilm; one of those two drugs, plus other antibiotics. So that's going on.
Are there patients in this country where you can't, for some reason, maybe a very old person who couldn't tolerate a surgery, as an example. Are they getting these drugs? Yes, they are, to try to spare them to have a surgery. With some success.
Q. Are these drugs done intravenously, or is it direc -- are they inoculated directly with the antibiotic right onto the implant?
A. Actually both are bio-available orally.
Q. Okay.
A. The fluoroquinolones and rifampin.

Q. But usually --
You agree with me that most like -- the standard of care and the most predominant treatment for a periprosthetic joint infection is a two-stage revision.
A. Usually that's --
MR. COREY GORDON: Object to the form of the question, --
THE WITNESS: Oh, okay. Sorry.
MR. COREY GORDON: -- lack of foundation.
A. I don't know if --
I think that is a standard. I don't know across the country how many people are doing that, but it's often happened --
Q. Okay.
A. -- that way.
Q. Now are you familiar with the preparation a patient goes through with respect to skin prep and draping for a total knee or total hip arthroplasty?
MR. COREY GORDON: Object to the form of the question.
A. I'm not a sur --
MR. ASSAAD: Basis?
MR. COREY GORDON: A, it's compound; B, you're -- it's a one-size-fits-all question. So if

he -- He can't answer a compound question, and he can't answer a one-size-fits-all question.
MR. ASSAAD: I'll -- Fair enough.
BY MR. ASSAAD:
Q. Have you ever seen a total hip surgery?
A. I haven't actually, no.
Q. Have you seen a total knee surgery?
A. No.
Q. Have you seen how a patient's prepped during those types of surgeries?
A. Only the, you know, the description that Dr. Mont gave at Science Day.
Q. Okay.
A. Very elaborate preparation.
Q. Okay. But you're aware of the types of skin preps that are used on these patients; correct?
A. You're talking about chlorhexidine alcohol?
Q. Yes.
A. Yes.
Q. Okay. And there's other types of -- of skin preps as well; correct?
A. Some people use iodophors.
Q. With alcohol?
(Interruption by the reporter.)
A. Today, Iodophor. And I think the tendency

is today if you're going to use an iodophor to use one with an alcohol.
Q. Okay. And in fact do you agree with me that the CDC has stated that there's really no difference between the iodophor with alcohol and the chlorhex with alcohol?
A. I'm not sure that's how they phrased it, but they recommend a prep with an alcohol.
Q. Okay. Whether or not it's chlorhex or iodophor.
A. Yeah. I think they opened the door to have io -- iodophor with alcohol --
Q. Okay.
A. -- in their recommendations.
Q. Do you -- Do you agree with the CDC recommendation?
A. Yeah. I actually think that -- that there's probably advantages of chlorhexidine alcohol over iodine alcohol, and that's based on the two MIMO studies that I cite.
Q. And you actually reviewed the CDC prevention -- Guideline For the Prevention of Surgical-Site Infection in preparation of your report; correct?
A. Yes.

Q. It's actually on Exhibit 2; correct?
A. Do you want me to go to that?
Q. Well it's on your -- on your list.
A. Okay. Yeah. Yeah.
Q. What is the mechanism -- Well, strike that.
Skin flora is on the skin and may be in the pores, correct, either the sweat glands or the follicles; correct?
A. Yes.
Q. Does it go any deeper than that?
A. Normally, no.
Q. Okay. So we have the -- we have flora that's on the skin and in the sweat glands and -- and the follicle -- the hair follicles and nowhere else.
A. And sebaceous glands.
Q. What are the sebaceous glands?
A. What are they?
Q. Yeah.
A. They're the glands that are primarily found that secrete -- they're also below the dermis. They secrete -- I have a picture of it, I think.
Q. I believe that's where we're going right now.
A. Yeah. And --
Do you want to wait and go to the picture?

MR. GOSS: 23?
Q. 23.
A. Yeah.
Q. Okay.
A. So do you want me to explain what sebaceous glands are?
Q. Well I asked --
So they're -- they're between the skin surface and the fat; correct?
A. Yeah. They're below the -- the dermis there, the -- the skin surface, right.
Q. And you're saying that bac -- that flora could be in the sebaceous glands?
A. There's no question about it. Propionibacterium acnes has been recognized to be there.
Q. And that's P. acnes?
A. P. acnes.
Q. Okay. But that's mostly found on the shoulders; correct?
A. Shoulder and back.
Q. And back, but not -- it's not -- it's not normally found in the knee or hip; correct?
A. It's very unusual to find --
Q. Okay.

A. -- infections with Propionibacterium --
Q. So would you agree with me that --
A. -- otherwise.
Q. -- that if a patient had P. acnes infection that it probably did not come from the patient, or if it did, it was through some sort of direct contact --
MR. COREY GORDON: Object --
Q. -- of a hip or knee?
A. Oh. Oh.
MR. COREY GORDON: Object to the form of the question.
A. No. I mean, it's not -- I think I've cited occasionally it can happen in either hips or knees, I forgot where.
Q. I think articles on shoulder surgery.
A. Pardon me?
Q. It was shoulder surgery that you were citing it to.
A. Yeah, but also if you look at Tande and Patel, I think I found 1 percent.
Q. How many percent?
A. One percent. So it's very low. In -- In either hips or knees, I don't remember which cite I had.
Q. But your --

But that could have come from -- I mean that -- there was no microbiologic study done in that case in which you know it came from the patient, it could have come from one of the staff members by direct contact.
A. There are no --
Not that I'm aware of any microbiologic studies to confirm that the same one came there. But, you know, we have sebaceous glands primarily in this area [indicating], but they're not zero other places of...
Q. I understand that. But if someone has P. acnes infection in the hip or knee, --
A. Yeah.
Q. -- I mean it's very unlikely that it came from them.
A. I don't know if it's unlikely.
Q. So you don't know one way or the other; do you?
A. That's right.
Q. Okay. You just don't know.
A. I don't know.
Q. Okay. So -- And just roughly how far does -- is the sebaceous gland and the hair follicle or the sweat gland underneath the skin surface?

A. I don't know.
Q. A millimeter?
A. I don't know. Never seen any data on that. I'm not sure.
Q. You don't know how thick the skin is?
A. No. Don't know.
Q. Okay. You've never --
A. Don't remember looking at it.
Q. -- never done -- in medical school did -- on a cadaver and cut through the skin?
A. I did -- I did do that, yeah.
Q. Okay.
A. Wasn't very far, but I don't know.
Q. I mean, are we talking two inches?
A. Probably not two inches. Less.
Q. An inch?
A. I don't know. I already --
Q. So you don't know?
A. -- told you I don't know.
Q. Okay. All right.
How far is it between the -- the sweat gland, which I think is the lowest, and a knee joint?
A. I don't know.
Q. How far is it between a sweat gland --
Well you agree the sweat gland look likes

it's the lowest in this picture here?
A. Well in the picture it looks like it's at the same level as the sebaceous glands roughly, so.
Q. Okay. Well let's just say whatever is lowest, how far do you think the bacteria is that's on a patient's skin or in the glands or -- from a knee joint?
A. I don't know how -- what the distance is in millimeters or not.
Q. Okay. Well you agree that there's no -- I mean, if a person is not -- doesn't have sepsis or an infection there's no bacteria in the fat; correct?
A. I think that's true.
Q. Okay. And --
A. No. No. Well in the fat, yeah. I think that's true.
Q. And you agree with me there'd be no bacteria in the muscle if a person doesn't have an infection.
A. Yes.
Q. Ongoing infection; correct?
A. If they don't have an infection?
Q. Ongoing infection, yeah.
A. Yes.
Q. Okay. And you agree with me that the --
(Interruption by the reporter.)

Q. And you agree with me that there's no bacteria in the blood if the person doesn't have some sort of blood infection.
A. By definition.
Q. Okay. Because in fact if someone had sepsis or a blood infection it probably wouldn't be a good time to do elective surgery; correct?
MR. COREY GORDON: Object --
A. To do what?
Q. Elective surgery.
MR. COREY GORDON: Object to the form of the question, also lack of foundation.
A. I don't think I understand the question I guess.
Q. Well if someone had an infection, an ongoing infection, --
A. Oh.
Q. -- it wouldn't be -- it wouldn't be proper to do --
A. Oh, I see.
Q. -- elective surgery.
A. I'm sorry. Didn't understand the que -- Yeah. I try to --
MR. COREY GORDON: Wait until he finishes.
THE REPORTER: Yes, please.

A. So to answer the question. One of the things that you want to do for any surgery that's elective is not to have any source of infection anywhere.
Q. Okay. So you mentioned that there is the -- the chlorhex with alcohol and the io -- iophorm [ph]?
A. Iodophor.
Q. Iodophor with alcohol.
What percentage of the bacteria do those prep solutions kill?
A. I don't think I know the answer to that, but a high proportion.
Q. 99.9?
A. I don't know.
Q. You don't know?
A. Might be, but I don't know. I can't cite any -- And if I answer you I want to try to cite the reference, that's what I'm saying.
Q. Okay. So sitting here today, you don't know.
A. No.
Q. Okay. And does it kill the bacteria that's in the -- the subacaneous -- or the sebaceous gland?
A. No, it doesn't.
Q. Okay. What about the sweat glands?

A. No.
Q. What about the hair follicles?
A. No.
Q. Okay. So is it your opinion that the most likely cause of a periprosthetic joint infection is that the bacteria is most likely coming from the -- either the sweat gland, the sebaceous gland or the hair follicle?
A. That's too general a statement. For example, the reason I say that, there are people who've done things like skin preps. You first -- You know, Daeschlein did a study just to look -- from Germany -- using an alcohol skin prep and he still finds bacteria in about 8 to 10 percent of people after the prep. And then during the surgery you can find more.
If I go back to the people who've looked at, let's say, shoulder surgery, first of all, you know, you saw from my report that I -- one study that was very large showed 21 percent of infections of the shoulder due to P. acnes. That's the implant. If you look at just rotator cuff we're talking 50, 55 percent of infections, rotator cuff, are P. acnes. If you look at spine repair for scoliosis, again about 50 percent are P. acnes. That's where the organism

lives.
Now if you -- peo -- I've -- I've quoted Sethi and Matsen and the -- a Japanese study that showed the organisms are there at the time of the incision, before the -- after the prep, before the incision. And Shiono's study with the spine and the back where they're repairing scoliosis. So 36 percent of the time after the prep they can find P. acnes. And then when they go in and actually look at the lamina, immediately exposing the lamina, it's already colonized in something like 25 or 35 percent.
So to me that comes back to the microbiome, back to the fact that we don't have a perfect skin disinfectant or antiseptic, rather, and the organism's there.
Q. For P. acne.
A. Yeah. That's the marker organism because it's hard to track, you know, a Staph epi, for example.
Q. Is there Staph epi in the hair follicles?
A. Not that I'm aware of, no.
Q. Is there Staph epi in the -- in the glands?
A. Don't think so.
Q. What about Staph aureus?
A. No.

Q. What type of bacteria are in the glands?
A. The one that I've talked about is P. acnes.
Q. Okay. So that's the only bacteria that you're aware of --
A. That's the only one that I'm aware of --
Q. Okay.
A. -- and it links to the --
Q. So would it be fair to say that if a person has a Staph aureus or a Staph epidermis or -- Strike that -- if a person doesn't have a P. acnes infection, that the most likely -- according to the most likely source of the infection would be from the skin and not the glands.
A. For Staph aureus, the source --
Q. Staph aureus, MRSA, Staph epidermidis. Everything besides P. acnes.
A. Yeah. Let me just refine a little bit.
So carriers of Staph in the nose are, you know, always at higher risk than non-carriers, two to three times fold for Staph infection. It turns out if you're a carrier in the nasal microbiome, you have a high chance of carrying it somewhere else, perineum, groin, axilla, as you know.
Q. And I'm just talk --
We're going to get there, and I promise you

we're going to get to the nose issue.
I'm talking about where we're looking at the skin here --
A. Yep.
Q. -- on page -- on -- I'm just trying to determine what's the most likely source of the different type of bacteria.
So if you look at page 23, okay?
A. Yeah. I've got it.
Q. The only bacteria that you are aware of that would reside in the glands or the hair follicles is P. acnes; correct?
A. That's all I know.
Q. Okay. So if a patient was infected with anything besides P. acnes, the most likely source, from looking at this picture, Figure 4 on page 23, would be the skin surface; correct?
A. That's my current hypothesis. I haven't seen a lot of studies. I can tell you about the sternal surgery for CABG with or without.
Q. Well I just want to know what your opinion is.
A. Yeah.
Q. I don't need to know your studies.
A. No. I'm just trying to say why I say what I

do or don't say what I do.
Q. So -- So my understanding is is that the skin prep, such as the chlorhex with alcohol or the other skin prep, would be able to reach the -- all the bacteria that's on the skin part of the patient's flora except for P. acnes; correct?
A. No, that's not true. They're ineffect -- They could reach the area.
Q. That was my question. They could reach it.
A. But they don't -- they're not effective in eradicating all the flora there.
Q. That wasn't my question. I said they could reach it.
A. Yeah.
Q. Correct?
They can't reach P. acnes because it's underneath --
(Interruption by the reporter.)
Q. They can't reach P. acnes because it's below the skin; correct? The -- The skin prep.
A. The currently used antiseptics don't reach --
Q. Okay.
A. -- down into the sebaceous glands.
Q. Okay. But they could reach the skin

surface; correct?
A. They reach the surface. It's put on the surface.
Q. Okay. And therefore the question is how much of the bacteria do they eradicate, the effectiveness of the skin prep; correct?
A. So say it again to make sure I got you.
Q. It reaches all the bacteria on the skin surface, the skin prep, the issue is what percentage of the bacteria it kills.
A. It's better to go back to the Darouiche study to say that if you start with a -- you know, an iodophor and compare it to chlorhexidine alcohol, chlorhexidine alcohol is a better, more effective skin prep than iodophor, reducing all surgical-site infections by 40 percent. Follow-up study with Tuul -- with Tuuli, thirt -- 45 percent, so it's very consistent.
Q. And you would agree with me that all those studies you're referring to are looking at superficial wound infections.
A. Well --
Q. "Yes" or "no"?
A. I'm trying to think whether there were any deep infections in those. I think Darouiche had some

deep infections. I don't --
Q. Which article are you --
A. -- I think --
Yeah. I thought that the Darouiche study on -- his first study that I've quoted here on -- Let me see if I can find the date. Comparing -- So I think it's -- Well, let me just not guess. (Witness reviewing exhibit.)
Wait. That'll be... So, you know, it's a New England Journal paper. Oh, I'm sorry. December 2010 New England Journal of Medicine.
Q. And can you point me to the page you're referring to?
A. I just remembered, so let me try to find the page I'm referring to.
MR. COREY GORDON: In his report, or in the article?
MR. ASSAAD: In his report.
A. Yeah, it's in my report. Okay.
So it'll be probably in the microbiome section.
Q. Would it be page 25?
A. Let's look. (Witness reviewing exhibit.)
Yes. And I thought he talked about both. My recollection he talks about some deep as well as

superficial.
Q. Are you aware that the surgeries that he looked at were colorectal, small intestinal, gastroesophageal, biliary, thoratic, gynecologic or urolo -- urologic operations?
A. Yes.
Q. None of them had to do with total hip or --
A. That's --
Q. -- total knee?
A. -- true.
Q. None of them had to do with implants; correct?
MR. COREY GORDON: Wait. Wait until he asks his --
A. That's true.
Q. Okay. So can you -- can you identify me today a study that shows that using a chlorhex with alcohol reduces the incident of a periprosthetic joint infection?
A. I don't think a study's been done just on the joints. I'm trying to remember.
Q. So sitting here today there is no evidence that a skin prep such as chlorhex with alcohol reduces the incident of surgical -- of periprosthetic joint infections; correct?

A. Well I would say there's no study out there, but if you take skin, the -- what we're really talking about is controlling the microbiome. And if you said to me today, I've got to get a hip replacement, I would tell you chlorhexidine alcohol, just as Dr. Reed did in his study, after awhile.
Q. You would agree with me that if -- if a -- Strike that.
If the bacteria comes from the patient's skin -- Let's take out P. acnes, okay? We could agree that P. acnes is a very unlikely cause of a infection for a total hip or total knee arthroplasty; correct?
A. Yes.
Q. Okay. Let's just assume all my questions is excluding P. acnes when I talk about bacteria going forward. Correct? Do you understand that?
A. If you want to make an assumption, yes.
Q. Yes. How does the bacteria get from the skin to the periprosthetic joint to cause an infection during the operation? If you know.
A. Well I have to go back to P. acnes, because it's the only study that shows that it's already there at the time of the incision, so it -- it's there. The other study I'd point to would be Tammelin's study of CABGs and Staph epi where he tried to do

fingerprinting to say if I look at the air, if I look at the surgeons and if I culture the patient's legs where the graft is for the CABG, or if I culture the sternum, he could find the only match that -- with any high numbers in the sternum for Staph epi. These are heart studies, but it comes back to what I've said earlier. If you have an organism, a marker organism and you can follow it, so he's able to do a fingerprint on those Staph epi on the sternum. I think I --

Q. Well I'm asking --

I mean, my understanding is, and it's a very limited understanding, that bacteria either need to be transferred by direct contact or they can be aerosolized. They don't have legs; correct? They don't move.

A. They can move, on the surface.

Q. How do they move?

A. I don't know how they move, but, you know, they're -- if there -- if there is an incision made across a group of bacteria, then why would you not think that they're actually going to fall into the wound? That's a hypothesis that I have --

Q. Is there any evidence --

A. -- but nobody -- nobody knows exactly how

they get from the flora to the wound. And I've said that in my report.

Q. Okay. So you have no opinion of how the bacteria get from the flora, patient's flora into the wound; correct?

A. Not in detail. I just know that they're already present at the time of the incision.

Q. Now do they jump from the patient's skin right into the -- into the joint, or would they go through the fascia and the mu -- and the muscle?

A. I don't know.

Q. Okay.

MR. COREY GORDON: Wait for him to --

THE WITNESS: I'm sorry.

MR. COREY GORDON: You gotta wait for him to finish the question.

THE WITNESS: Yeah. Apologize.

Q. Okay. So --

And you're aware that in many total hip and total knee arthroplasties, if not all, that patients are given a prophylactic dose of antibiotics.

A. Patients are given antibiotics, yes, preoperatively, perioperatively.

Q. Perioperatively. Actually before even incision.

A. Yes.

Q. Okay. And in fact that has shown to reduce the incident of superficial wound infection for total hip and total knee arthroplasty; correct?

A. More than that. I mean, if I go back to Lidwell's study, he -- when he looked at the patients who had perioperative antibiotics, their deep-joint infection rate was four times greater in the group that didn't have antibiotics.

MR. COREY GORDON: You said "greater."

THE WITNESS: I'm sorry.

A. The people who didn't get perioperative antibiotics had a four times risk of the prosthetic joint infections compared to the ones who did.

Q. So we agree that perioperative antibiotics decreases the risk of periprosthetic joint infections?

A. Yes.

Q. Okay. You do agree with me that the bacteria has to get to the -- to the joint area to cause a periprosthetic joint infection perioperatively; correct?

A. Bacteria are necessary, not sufficient, yes.

Q. Okay. And when we say "get to the joint area," we're getting to the prosthesis during the total hip or total knee arthroplasty; correct?

MR. COREY GORDON: Object to the form of the question.

A. I don't know exactly, you know, does it start above and then get moved to the joint, but that could happen, yeah.

Q. But for the biofilm to form it has to be in the prosthesis.

A. Yeah, it has to be on a foreign body. Well I think in --

Q. Most likely.

A. I think it's more likely, you know. In some chronic wounds they've shown biofilm. You probably know that.

Q. But with respect to total hip and total knee --

A. Yeah.

Q. -- the bacteria has to get to the prosthesis to form biofilm; correct?

A. I think that's right.

Q. Okay. So during the operation it's your opinion that a bacteria on the patient's skin gets to the prosthesis at some point in time to cause an infection -- to cause a periprosthetic joint infection.

MR. COREY GORDON: Object to the form of

the question.
A. So I think the source of al -- of almost all infections, including periprosthetic joint infections are the patient's flora, and again the skin would be the site primarily.
And I'm not sure that I understood the complex question.
Q. Well the bacteria that's on the patient's flora has to reach the -- the --
A. Has to get to the area --
Q. -- the prosthesis --
A. I'm sorry.
Q. -- has to get to the prosthesis during the operation.
A. Yes.
Q. Okay. Now when we talk about where the bacteria's coming from, are you talking about the skin where there -- it's been prepped and where the surgical site is, or are we talking about the fa -- the bacteria that's on the face of the patient that's underneath the drape?
A. I think, my -- my feeling today, is that it's primarily in the skin near the incision, and again the P. acnes studies would actually demonstrate that.

Q. Okay. Now with respect to people that are carriers for MRSA or MSSA in their nose, okay, the --
What's the correct word? What is the correct word for that?
A. You talking about a nasal?
Q. Yeah.
MR. COREY GORDON: Nares?
A. Nares?
Q. Yeah, the nares.
And you've talked about that in your report; correct?
A. Yeah.
Q. They're carriers; correct?
You're not offering the opinion that the bacteria in the nose is actually reaching the surgical site and the prosthesis and causing an infection; are you?
MR. COREY GORDON: Object to the form of the question.
A. What I think happens is that if you're a carrier in the nose you're frequently a carrier elsewhere on the body; it can be in the hands, as shown by Reagan, et al. If you want to look at Mermel and colleagues, it's carried in the groin and the perineum and axilla as well.

So if you look at all the people who are carriers of Staph, the most sensitive spot is going to be in the nose. We also know that there are carriers of, you mentioned MRSA, 15, 20 percent carry it only in the throat. And again I think that the nose is a marker for the increased likelihood of carriage in other places of the body.
Q. What's the likelihood that if you have MRSA or MSSA it's going to be on your knee?
A. The knee? I don't known. I haven't seen data.
Q. There's no evidence that -- that the fact that you're positive in your nose or even throat, means that you have MSSA or MRSA on your knee; correct?
A. No. But if it's the groin and you're talking about hip, for example, or a knee, is it possible? Could it happen? I don't -- can't cite a paper.
Q. But the groin is isolated during the surgery; correct?
A. It is isolated. I don't know how effective that is.
Q. Okay. Do you know what -- whether or not the drapes are permeable or impermeable in an

operating room?
A. No, I don't. I haven't looked at that.
Q. Okay. But you're not saying, just so I understand you, that if you have MRSA in the nose or MSSA in the nose, that as the patient breathes out that bacteria is coming out of your nose and infecting the prosthesis.
A. I don't know how if --
Let's say, imagine in a scenario that we're just making up to have the discussion, it's a carrier only in the nose. How it gets from the nose to the wound, I don't know completely. Is it possible that that could happen? Maybe. I don't know. There are no studies that show the organism in the nose can't move, can't be blown out.
Q. Okay. You do understand that in a total hip or total knee arthroplasty there is a huge drape that goes three feet above -- two to three feet above the patient; correct?
A. Yes.
Q. Okay. That separates the head of the patient --
A. That's right.
Q. -- from where the surgical site is; correct?
A. Yes. Sorry.

Q. And you agree with me that --
So are you saying that it's possible that the bacteria could come out of the nose and over the drape or around the drape and into the surgical site?
A. I don't know.
Q. Okay.
A. I mean, I... I know that people who have colds certainly disperse when they sneeze or cough or something, with Staph.
Q. But if the ventilation is doing what it's supposed to be doing, it would push the bacteria down; correct?
A. I think so.
Q. Okay. Unless there was something else out there that was causing the bacteria to go up; correct?
A. I think so.
MR. ASSAAD: Let's take a break.
THE REPORTER: Off the record, please.
(Recess taken from 1:50 to 2:05 p.m.)
THE WITNESS: Can I make just a -- you asked -- said earlier you didn't mind, Mr. Assaad, if I made changes, and just on break looked up the microbiome of the sebaceous glands, and in fact I can point to a reference for you, General Clinical Micro 1984, Leeming. And in addition to P. acnes,

Propionibacterium, both Staphylococcus, they didn't differentiate epi and aureus in the brief summ --
(Interruption by the reporter.)
THE WITNESS: -- epi from aureus, and also Pityrosporum. So I want to add that to my statement, and thank you for letting me amend.
BY MR. ASSAAD:
Q. Do you know how prevalent the Staph --
A. No. I have to do a lot more looking at it, but --
THE WITNESS: I'm sorry.
MR. COREY GORDON: Let him --
Q. So sitting here today, you don't know, like, what percentage or -- or where in the human biome they did the sampling.
A. They -- They sampled the sebaceous glands.
Q. But where?
A. I don't know.
Q. Could it have been on the shoulder or back?
A. Well you're asking me questions I don't know, --
Q. Okay.
A. -- but I gave you a reference and wanted to clear up the fact that Staphylococci can live there.
Q. What's the name of the reference?

A. General Clinical Micro, 1984, Lemming, L-E-M-M-I-N-G. I don't have the first initial.
Q. Lemming, L-E-M-M-I-N-G?
A. Yeah.
Q. Okay. Do you know who doctor --
MR. GOSS: It's actually L-E-E-M-I-N-G.
THE WITNESS: Oh, I'm sorry. Did I get that wrong?
Q. And you just looked that up where?
A. Yeah. Just now.
Q. On your phone?
A. I used his phone.
Q. Okay. You're pointing to Peter Goss?
A. Yes, Peter Goss.
Q. Did he provide the article to you?
A. He did.
Q. Okay. So you didn't look it up, he just gave --
A. I did. We were both looking things up just to check.
Q. Well who pulled up the article; was it you --
A. He did.
Q. -- or Peter Goss?
A. He did. Peter did.

Q. Okay. So my understanding is that while I'm asking you questions Peter Goss is doing some research for you during this deposition?
A. Yeah, I guess you could say that.
MR. GOSS: Object to form.
A. He just checked a reference for me. I was trying -- We were both trying to find stuff.
Q. All right.
Do you know who Dr. Reed is?
A. Doctor who?
Q. Reed. Michael Reed?
A. I don't know him, but I know who he is, yeah. He's --
Q. Okay. Are you aware he's doing a pilot study for 3M right now?
MR. COREY GORDON: Object to the form of the question.
A. I think that came up earlier, and I think I had heard that it might be, but I don't have any evidence or, let's say, direct knowledge of that.
Q. Do you know Dr. Harper?
A. No.
Q. Have you read any of his literature?
A. Don't think so.
Q. Okay. So have you read Dr. Reed's

deposition?
A. I think so, yeah.
Q. Have you read Dr. McGovern's deposition?
A. Yes.
Q. Have you read Dr. Legg's deposition?
A. I think so, yeah.
Q. Have you read Dr. Nachtsheim's deposition?
A. No.
Q. Have you read Dr. --
A. I don't remember. I may have, but I don't remember.
Q. Have you read Dr. Legg's deposition?
A. I think so.
Q. So -- And you're aware, from reading articles by Dr. Reed, that he has written articles critical of the Bair Hugger safety; correct?
MR. COREY GORDON: Object to the form of the question.
A. I'm not sure which articles you're referring to.
Q. Well McGovern was -- Dr. Reed was on that; correct?
A. Yes.
Q. And you're aware that actually Dr. McGovern would be -- was more -- or Dr. Reed was more senior

than Dr. McGovern at the time.
A. That was my understanding.
Q. He was more of the advisor and overlooking the whole study; correct?
A. Yeah.
Q. Okay. And you know that --
Are you aware that at one time Dr. Reed was in Minneapolis and wanted to talk to the people at 3M to discuss his findings?
MR. COREY GORDON: Object to the form of the question, and assumes facts not in evidence.
A. I had heard that possibility, but I don't know anything about that.
Q. And are you aware that 3M didn't want to talk to him?
MR. COREY GORDON: Same objections.
A. I don't know that.
Q. Okay. Well I'm going to read you what the objective of the study was, and tell me if it's...
MR. COREY GORDON: You talking about McGovern?
MR. ASSAAD: No. The pilot study.
MR. COREY GORDON: Oh.
Q. Strike that.
Are you aware that 3M is funding a pilot

study in which they are assessing the risk of postoperative orthopedic implant infection which may be influenced by the choice of the intraoperative warming technology?
A. I don't think I know that, no.
Q. Okay. Would that be information helpful to you to see what the -- the data in that study, to formulate your opinions of whether or not the Bair Hugger has an effect on periprosthetic joint infections?
A. So I don't --
What was the hypothesis of the study? And you're asking me to --
Q. The hypothesis is this: We postulate that the risk of postoperative orthopedic implant infection may be influenced by the choice of intraoperative warming technology. We plan to investigate this through a multicenter superiority trial comparing forced-air warming and resistive warming in adults undergoing hemiarthroplasty following hip fracture. Health/economic evaluations will form the secondary aim of this study.
Are you aware that 3M is provi -- funding a study?
A. No.

Q. Is that the type of study that might be helpful in determining whether or not forced-air warming has an effect on periprosthetic joint infection?
MR. COREY GORDON: Object to the form of the question.
A. Hard to know, but I love information. So if you tell me there's more information out there, I'd love to see it.
Q. Do you think a company should suppress research regarding the safety of a device if there is liti -- ongoing litigation regarding that device?
A. So hypothetically if there's ongoing litigation a company tries to suppress?
Q. Research.
A. And this is hypothetical?
Q. Yes. Hypothetically.
A. Yeah.
Q. You think that's okay?
A. I don't think --
Q. Regarding the safety of a device.
A. Huh?
Q. Regarding the safety of a device.
A. Regarding the safety, hiding data?
Q. Or -- or not -- or not --

Or suppressing research.
A. Oh, suppressing research. I don't know the details of what you're getting at here.
Q. Okay.
A. You're trying to say somebody suppressed research maybe.
Q. Well hypothetically speaking, if a -- a decision was made by 3M not to perform any research regarding the safety and efficacy of the Bair Hugger during this litigation, would you consider that being responsible by a corporation?
A. Well I think the question is really do they have information already on the safety and efficacy of the Bair Hugger, and will this add more and they will need it. I don't know. I'd like to see the whole thing laid out and what the circumstances are for or not.
Q. Can you identify one study that indicates that the Bair Hugger does not cause periprosthetic joint infections?
MR. COREY GORDON: Object to the form of the question.
A. "Does not cause."
So I've put in my report, you know, I think everything from the two clinical trials, but

periprosthetic. Certainly warming, I showed you the study, I guess, from Holland.
Q. I'm just ask --
I'm asking one question.
A. Yeah.
Q. Just identify a study that indicates that forced-air warming or the Bair Hugger does not cause a periprosthetic joint infection.
MR. COREY GORDON: Object to the form of the question.
A. Yeah. I mean, I can't come up with an answer for that right now.
Q. Okay. And are you awa --
You've read Dr. Kurz's deposition; correct?
A. I have.
Q. You're aware that she told 3M that her 1996 study only applies to colorectal surgeries.
MR. COREY GORDON: Object to the form of the question, misstates the evidence, assumes facts not in evidence.
A. Don't remember what she told 3M, but that's -- that's the study that she did was colorectal patients.
Q. And it only applied to colorectal patients; correct?

MR. COREY GORDON: Object to the form of the question.
A. I don't know that she said that but, you know, if she said I'm not sure that that would be so.
Q. And you're aware that Dr. Augustine and Dr. Sessler used that information and marketed the Bair Hugger across the world to increase sales.
MR. COREY GORDON: Object to the form of the question, and assumes facts not in evidence.
A. I'm not aware that they did that, but if that was the best data, and again if I --
Q. Well you love data, don't you?
A. I love data. That's why I'm saying it, for you. If I -- You know, if I said to you, look, here's a device that cuts down your infections by two thirds, you're saying, well I'm getting a little different operation than that one, I would still advise you this is the best data.
Q. Where do you get that it cuts down by two thirds?
A. You mean the Kurz study?
Q. Yeah.
A. Yes, 15 percent in five, I'm off by maybe a little bit.
Q. Okay. And -- And you heard her say recently

that -- that that study would not be scientifically valid today; correct?
MR. COREY GORDON: Object to the form of the question and misstates the testimony.
A. I actually read the whole response that she said, and then later on she was questioned. Did you -- And she said, did I really say that? Because I -- You know, then she went on to say, I would need a bigger study because, you know, so many things have been done and everybody has to have a warmer. And the second thing, she said it may not be two thirds, she said 30 percent reduction is probably what I would see today.
Q. In colo --
A. Still humongous, she said.
Q. Do you think there's a difference between colorectal surgery and -- and a knee surgery?
MR. COREY GORDON: Object to the form of the question.
A. Of course there's a difference, I mean. But if you said does the skin react differently, you know, or the microbiome, the body's physiology whether a knife is on the abdomen or on a hip, I'm not sure.
Q. You think, sitting here today, that the primary source of the bacteria in a colorectal surgery

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which has a high incidence of infection, is the skin and not the colon?
A. Well they had both, actually. When you look at the organisms, if you found a Staph aureus, which they certainly found, that was part of the finding. That's not an organism commonly in the GI tract. Can be. They also found enterococcus, they had one candida. So they certainly had a mixture of what was in the GI tract and what was on the skin. So if that's what you're asking, yes.
Q. I mean you agree with me that colorectal surgery has a high incidence of infection because it's a -- whether it's a clean contaminated or a contaminated surgery; correct?
A. That is correct.
Q. It's a much different surgery than a total hip and total knee, --
A. It's --
Q. -- which is a clean surgery.
A. It's different from those operations, yeah. But what I'm saying --
Q. Well that's all I -- that's all I need.
A. Okay.
Q. So, I mean, we agree that total hip and total knee are considered clean surgeries.

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A. Yes.
Q. Okay. With respect to the Leeming -- Leeming article that we just referenced, are you aware that the biopsies of the skin were taken on the back?
A. No. I did -- you know, we -- this was a very quick look and wanted to see the punch line.
Q. So you would agree with me that just assume that I'm reading this correctly, that the samples were taken on the back skin -- okay, the back -- the back skin, that that doesn't indicate that there's data that these types of bacteria are on the glands in the knee or hip; correct?
A. If that's true, then that's what the study would say.
Q. Okay.
A. I'm not questioning your...
Q. All right.
(Mr. Ben Gordon departed the proceedings.)
Q. And as an expert that's doing a literature review, the best evidence to rely upon are going to be peer-reviewed studies; correct?
MR. COREY GORDON: Object to the form of the question.
A. In general I think that's better.
Q. Because there are many studies that are

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performed, even internally at 3M, that they might just be trying to determine which is the best way to study and might try different types of techniques; correct?
A. Yeah, I don't know what 3M's doing in trying to come up with techniques.
Q. But, for example, let's talk about, you know, culturing glands, okay? Let's see what grows in glands. There might be some techniques that work to determine whether or not there's bacteria in the glands, and there might be other techniques that might not work; correct?
MR. COREY GORDON: Object to the form of the question.
A. Hypothetically, yes.
Q. And as a scientist you're trying to determine, you know, if you want to collect data, which is the best way to collect data; correct?
A. I'd like to know the best way always.
Q. Okay. And sometimes you might try a method that might not work; correct?
A. Happens all the time.
Q. Okay. Happens all the time.
And when you try a method that doesn't work, do you publish that?
A. You might.

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Q. You may if you've gone through a whole study; correct?
A. You might.
Q. Okay. But you might not publish it; correct?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.
A. I don't -- I don't know. I -- If you're getting to the maybe seven studies that were done by Dr. Reed and Dr. -- and his colleagues that were not published that were important data, then I probably won't agree with you.
Q. Oh. So you could have unpublished data that's important?
A. I guess what I'm saying is --
Q. Is that what you're saying?
Answer my question, please?
MR. COREY GORDON: He's about to answer your question.
A. No. I'm trying --
MR. COREY GORDON: Don't cut him off.
A. I'm trying to answer your question. So let's go back to --
MR. ASSAAD: Simple question.
A. Let's go back to particles --

MR. ASSAAD: A very simple question.
Q. Okay. I'm talking to my colleague.
A. Yeah, that's fine.
Q. I'm just saying it was a simple question, but you go ahead and answer.
A. Okay. So, you know, one of the studies, you know, a series of studies that looked at particles as opposed to bacteria. And the real question is just, you know, you might find more particles, you might find more heat, you might find, you know, smoke, for example, but if the -- the question then is, do -- are the particles actually associated or linked with the colony-forming units.
So in my report I have eight studies that show that no obvious signal, at least with the Bair Hugger in use, that you're going to get colony-forming units. And then through discovery find out that there were seven studies, you know, for the other side, if you will, that were not published that also showed you cannot find colony-forming units when the Bair Hugger is in use.
So when you say that -- that the peer-reviewed literature is important, I totally agree, I want that. But if there are other studies, and I've shown you the seven, including ones where the

authors said, look, we tried three different ways in five different studies to try to find colony-forming units when the Bair Hugger was working, we couldn't. So collectively I think those are use -- useful data.
Q. Did you look at the studies?
A. I did.
Q. Okay. And they were not peer reviewed; correct?
A. Don't even know I -- whether how many were even sent for peer review. You mean the seven that I'm talking about?
Q. Were you provided any studies from 3M internally?
A. No.
Q. Okay. So 3M just provided you the studies to call -- talk about hidden studies of actual researchers that are trying to solve a problem, and they did not provide important internal studies that they have; correct?
A. Well --
MR. COREY GORDON: Object to the form of the question.
THE WITNESS: Yeah.
A. Well I guess what I found out about the studies was primarily through the depositions.

Q. That wasn't my question. Just please answer my question.
A. Yeah.
Q. Did they provide you studies or not?
A. Okay. Look. Maybe I didn't understand. Go ahead.
Q. Did they provide you internal studies? Just answer my question, sir.
MR. COREY GORDON: Asked -- Objection -- (Interruption by the reporter.)
MR. COREY GORDON: Objection, asked and answered.
Q. Did they provide you any internal studies?
MR. COREY GORDON: Objection, asked and answered.
MR. ASSAAD: Fair enough.
A. So internal studies, I don't think I saw anything from 3M.
Q. And please, doctor, listen to my questions.
A. I'll try better.
Q. We have very few hours left. Let's not try to go on tangents.
Are you aware that 3M manipulated particle data that they -- on a study that they funded?
MR. COREY GORDON: Object to the form of

the question, assumes facts not in evidence.
A. Don't know anything about that.
Q. So 3M did not provide you the data that they did particle tests out in Holland?
MR. COREY GORDON: Same objections.
A. I don't have that data.
Q. Okay. Are you surprised that that data exists?
MR. COREY GORDON: Same objections.
A. I don't know how to answer that. I have -- just haven't gotten it yet.
Q. Are you aware that 3M funded a study to do the effects of the Bair Hugger on particles in a laminar operating room?
A. No.
Q. Did you do independent research to determine whether or not there were particle tests conducted on the Bair Hugger?
A. Did I do research?
Q. Yeah.
A. No. I -- Everything that I did is in my report.
Q. So you did not do any PubMed searches or researches to search with particle tests for a Bair Hugger?

MR. COREY GORDON: Object to the form of the question.
A. Yeah, I did. I -- I think I have those listed.
Q. You don't have the Dr. Sessler and Russ Olmsted study; do you?
A. No, I don't think so.
Q. Okay. So the one study that was funded by 3M, you don't have.
A. Correct.
MR. COREY GORDON: Object to the form of the question.
THE WITNESS: I'm sorry.
Q. That was done in 2011. You don't have that study.
A. I don't think I have that study.
Q. Okay. Are you aware that 3M has relied heavily on the Sessler study in trying to market the Bair Hugger device and its safety?
MR. COREY GORDON: Object to the form of the question, also assumes facts not in evidence.
A. No, I don't know any of that.
Q. Doctor, you are aware that many orthopedic surgeons care about increase of particles in -- above the surgical site.

MR. COREY GORDON: Object to the form of the question, also lack of foundation.
A. I don't know what they think about particles, no.
Q. I mean, have you worked with orthopedic surgeons in the past?
A. Only clinically --
Q. When you say clini --
A. -- where you take care of their patients.
Q. After they've had the infection; correct?
A. That's correct, yeah.
Q. Okay. Do the numbers of bacteria arriving in the surgical wound correlate directly with the probability of surgical-site infection?
A. Well I would point to Stocks article first, and he has a correlation for those particles that are greater than 10 microns in size. And then there is the study we talked about, the Darouiche study, that modeled bacteria and particles.
Q. So you agree with Stocks' paper?
MR. COREY GORDON: Object to the form of the question.
A. Let me -- Let me -- Let me finish.
You know, and then there's Birgand's study who in fact shows the correlation between -- in

general between particles and bacteria. But he also did something else, he looked at the relationship between the number of particles in the air and the contamination of the wound. That did not correlate at all. So Birgand talked about those studies in his article that there were many that showed a correlation and also many that didn't show a correlation.
Q. So can you answer my question "yes" or "no"? I want to know what your opinion is, not what other people say.
A. No. I understand. I mean I'm --
MR. COREY GORDON: Let him finish his --
Q. I could read their -- I could their articles.
A. Yeah.
Q. My question is: Does Dr. Wenzel, you, do you agree that the number of bacteria arriving in the surgical wound correlate directly with the probability of surgical-site infection?
MR. COREY GORDON: Object to the form of the question, move to strike counsel's commentary.
A. So when you say those, you're talking about the studies that correlate particles and bacteria are those that land in the wound, --
Q. I am talking --

A. -- you're saying?
Q. -- about -- not the studies, I'm talking about what Dr. Wenzel's opinion is.
A. Yeah.
Q. Okay. Based on what whatever you've read.
A. Yeah.
Q. Okay. I don't want to know the studies, I know what the studies are. Because I know some of them you agree with and some of them you don't agree with; correct?
A. That's right.
Q. Okay. So I want to know what your opinion is, not what the studies' opinion is.
A. Umm-hmm.
Q. Fair enough?
A. Yeah.
Q. Okay. Does Dr. Wenzel agree, you, that the number of bacteria arriving in the surgical wound correlate directly with the probability of a surgical-site infection?
A. I can't answer that for all studies, there is a disparity of that. But my opinion is that it's not been linked to surgical-site infections. Particles and bacteria have been linked, but not necessarily that link of CFUs and infection.

Q. I wasn't talking about particles.
Listen to the question.
A. Yeah. Go ahead.
Q. Do the numbers of bacteria arriving in the surgical wound correlate directly with the probability of surgical-site infection; "yes" or "no"?
A. Well Birgand would say no, he can't find a correlation with contamination of the wound.
Q. What about Dr. Wenzel?
A. I don't know.
Q. Okay. You don't know.
A. I mean, I'm not sure.
Q. Okay. What about this question: Do the number of bacteria in the operating room environment correlate directly with the probability of SSI, "yes" or "no," according to Dr. Wenzel?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical. It's not a yes-or-no question.
Q. "Yes" or "no"?
A. So the total number of bacteria in the air?
Q. I'll read it again.
A. Yeah.
Q. Do numbers of bacteria in the operating room environment correlate directly with the probability of

surgical-site infections?
A. I haven't seen that, no.
Q. So you disagree --
A. I don't know.
Q. -- with that.
A. I don't know.
Q. You don't know. Okay.
You don't have an opinion whether or not OR traffic increases the risk of surgical-site infection; is that correct?
A. I think in general OR traffic's been linked to increasing particles. It's hard to know whether those increased surgical-site infections, but I think there are some studies. I'm having trouble remembering which ones show that it might, but it might be important. But then there is some contradictory evidence and I was just, in my report, trying to show that.
Q. Well just so I understand, at trial you're not going to have an opinion that OR traffic caused a surgical-site infection.
MR. COREY GORDON: Object to the form of the question.
A. At this point I don't know. Yeah.
Q. Well I --

A. Yeah.
Q. -- here's the thing, doctor, and I'm not trying to be difficult. I know the studies as well as you do.
A. Yeah.
Q. Okay. And -- Not as well, but I know them fairly well. You probably know them better.
I'm not -- I could read the studies as well. I want to know based on your reading of the studies what Dr. Wenzel's opinion is, okay? Not what the literature says, but what your opinion is. You could support it with the literature, but at this point in time I've read your report, I know what literature you're relying upon.
I just want to know, okay, do you think that OR traffic increases the risk of surgical-site infections in a total hip or total knee arthroplasty?
A. It might, yes.
Q. It might --
A. Yeah.
Q. -- or it does?
A. I don't know. It might.
Q. Can you say that within a reasonable degree --
A. Yeah.

Q. -- of medical probability?
A. Yeah, I think so.
Q. Okay. So if that's the case, then you have to agree that the -- the OR traffic increases particles, and therefore increases the bacterial load in the operating room; correct?
MR. COREY GORDON: Object to the form of the question.
A. According to some people who've shown correlations.
Q. Well do you agree with that?
A. They'll show correlations with particles and CFUs in some studies, and I've already talked about those.
Q. I'm just saying with the OR traffic.
Do you agree that the OR traffic has -- has an effect on surgical-site infections in total knee or total hip arthroplasty?
MR. COREY GORDON: Object to the form of the question, --
A. It might.
MR. COREY GORDON: -- also asked and answered.
Q. It might. Okay.
And it may not; correct?

A. Yeah.
Q. Okay. So sitting here today you don't know one way or the other.
A. Yeah.
Q. Okay. Going on.
Do you agree that the incidence of periprosthetic joint infection is related to surgical time?
A. Surgical time has been shown to be a risk factor, yes.
Q. So Dr. Wenzel agrees with that.
A. Yeah.
Q. Okay.
A. I have a example of that in my section on risk factors.
Q. Do you agree there still needs to be further research with per -- with respect to the effects of hypothermia on periprosthetic joint infection?
MR. COREY GORDON: Object to the form of the question.
A. Well, you know I love data. Any more information that would be added to what I -- what we have here, I'm always -- I mean, there's never -- I'm never going to say, no, don't do a study.
Q. I understand that.

But you're not going to do a study if you know the answer; correct?
MR. COREY GORDON: Object to the form of the question.
Q. You do a study to find out the answer.
A. Yeah, you do, and -- but you always want confirmation, I think. I guess that's what I'm saying.
Q. I understand that. But are you -- But sitting here today you cannot state, with any degree of medical certainty, that maintaining normothermia reduces the incident of periprosthetic joint infection because that has never been looked at; correct?
MR. COREY GORDON: Object to the form of the question.
A. So that part is true, they haven't studied just joints in a prospective way, yes.
Q. So further research would be needed to answer that question.
A. Further research would really help answer it.
Q. Okay. Are you aware that 3M never did a safety validation of the Bair Hugger device?
MR. COREY GORDON: Object to the form of the question, lack of foundation, assumes facts not

in evidence.
A. I'm not.
Q. Are you aware that the Bair Hugger device was based off a 1937 cast warmer?
MR. COREY GORDON: Object to the form of the question.
A. No, I didn't know that.
Q. Okay. Are you aware that the older Bair Hugger device warned for air -- airborne contamination?
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence.
A. Say that again.
Q. That the older version, the mod -- the series 200 Bair Hugger devices warned about airborne contamination?
MR. COREY GORDON: Same objections.
A. And I don't know that. I don't re --
Q. Are you aware that competing products of the Bair Hugger, such as the Mistral, that are forced-air warming, warn about airborne contamination?
A. Don't know that either.
Q. Would that influence your opinion in any way?
A. I'd have to see what they say.

Q. Okay. But the --
But 3M has not shown you that information; correct?
A. I haven't seen that.
Q. And you love data; correct?
A. I do.
Q. I mean, you -- the more data the better for you; right?
A. I like it.
Q. I mean, you spent over 300 hours going through data; correct?
A. That's true.
Q. And if you had to do a hundred hours more you would do it; correct?
A. I love it.
Q. Love data.
And if 3M gave you more data you would have reviewed it; right?
A. I would.
Q. Okay. And so sitting here today do you agree with me that there is some data that 3M did not provide you?
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence, lack of foundation.

A. I don't know that.
Q. Okay. Are you familiar with the international consensus of orthopedics that discuss periprosthetic joint infections?
A. I don't think I know that.
Q. It was sponsored by 3M.
MR. COREY GORDON: Object to the form of the question, mischaracterizes the evidence.
A. You're asking if I know that? I don't.
Q. Okay. Do you know who Dr. Parvizi is?
A. I know who he is, yeah.
Q. Okay. Do you know --
You know Dr. Gregory Stocks; correct?
A. I don't know him, no.
Q. But you've read his -- his -- you know who he is.
A. Yes.
Q. Okay. And you've actually cited to one of his articles; correct?
A. I did.
Q. Okay. And you would consider him an expert in orthopedic surgery; correct?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. I don't know if he's an expert or not in

orthopedic surgery.
Q. Are you aware that the general consensus among orthopedic surgeons have the opinion that periprosthetic joint infections are caused by airborne contaminants?
MR. COREY GORDON: Object to the form of the question, lack of foundation, mischaracterizes, assumes facts not in evidence.
A. No, I'm not aware of their general opinions.
MR. ASSAAD: Let's take a break.
THE REPORTER: Off the record, please.
(Recess taken from 2:45 to 2:55 p.m.)
BY MR. ASSAAD:
Q. One of your critiques of the McGovern study was the change in anti -- the prophylactic anticoagulant; correct?
A. Yes.
Q. Okay. Are you aware of any studies that compared the two -- the two drugs used in McGovern for anticoagulation and compared with infection rates?
A. I thought that Brimmo's study actually looked at the two, Rivaroxaban versus other anticoagulants.
Now, you know, did -- your question partly was did it go only with enoxaparin. I don't think so.

I think there were options. The infection rate of course was two and a half percent versus .2 percent -- or the, you know, with rivaroxaban the high number, and the other anticoagulants .2 percent, which was significant.
So independent of the McGovern study I guess there were two parts of that study. I mean, Jensen's study was separate, and he found two and a half percent versus I think one percent, again with rivaroxaban. And then somewhere along the line, I think it was Albrecht who said, if you keep the antibiotics constant you get something like 4.2 percent versus 1.7 percent.
So these are the data that come to mind comparing rivaroxaban versus enoxaparin, or rather the -- the alternative.
Q. Are you awa -- Okay. Let's go to your Exhibit Number 2, your Exhibit B.
A. What am I going to?
Q. Your document list.
A. Oh.
Q. And you mention the Berrios-Torres article, Centers for Disease Control and Prevention Guideline For the Prevention of Surgical Site Infection 2017 as being authoritative?

A. Which number is this?
Q. Exhibit Number 2.
A. I'm sorry.
Q. It's a list of documents you considered.
A. Yeah.
Q. Remember we talked about the CDC?
A. Yeah.
Q. Okay. And you thought it was authoritative?
Are you aware that in this article it states, high-quality evidence suggested no difference between injectable enoxaparin and oral rivaroxaban and risk of SSI?
A. I think I do remember that, yeah.
Q. Okay. And you're disregarding that.
A. No, I'm not -- I wouldn't disregard anything.
Q. And this was based on no difference in SSI in a large meta-analysis, 12,383 patients of four, random controlled trials in elective primary or revision total hip or total knee arthroplasty, and no difference in hemorrhagic wound complications or drug-related adverse effects.
Do you disagree with that or agree with that?
MR. COREY GORDON: What are you reading

from?
Q. He knows where I'm reading from.
A. So I think you're referring to the capital studies, or what are they called, the RECORD studies, I guess. Is that the reference that you're talking about, CDC said that?
Q. They're referring to --
A. The four large studies?
Q. Eriksson, Kakkar?
A. I think they're all part of the RECORD studies.
Q. And do you disagree with the CDC?
A. Well I think I have to clarify that, because Jensen did a study, and he said unfortunately the RECORD studies didn't do a very good job looking at surgical-site infections, and that's why -- that's prompted him to do a study.
Q. So you disa --
A. And Bremo --
Q. You disagree with the CDC.
A. I think it needs some clarification, in that sense.
Q. So --
But you disagree with their statement that high quality -- high quality --

A. Yeah.
Q. -- evidence suggested no difference between injectable enoxaparin and oral rivaroxaban and risk of SSI.
Do you agree or disagree with the CDC?
A. So that's what they found, that's what they believe. I was just trying to clarify, and I don't necessarily disagree with them, I have a different interpretation based on, you know, the studies of Jensen and Brimmo.
Q. What was the number of people in those populations in Jensen?
A. They were -- They were much smaller than the thousands in this.
Q. 12,383.
A. Yeah.
Q. Okay.
A. But -- But again, I just want to point out, when Jensen opens up his article he said, look, we don't have a good handle on surgical-site infections. They focused on bleeding, they focused on which was a comparable or a different thromboprophylaxis from the point of view of a DVT or a pulmonary embolus. And then Borak, when he was asked similar questions, said he couldn't even find the definition that they used.

And so it comports with the same finding that Jensen said in his study, and the same for Brimmo. They both think that --
Q. What's Dr. Wenzel's opinion? Does -- Is there a difference in the risk of surgical-site infection between rivaroxaban and enoxaparin?
MR. COREY GORDON: You're asking about enoxaparin, --
A. Yeah. Not --
MR. COREY GORDON: -- not tinzaparin.
A. Yeah.
Q. I'm asking.
A. Yeah. I mean, in those studies CDC is probably right.
Q. And you're aware that the CDC put enoxaparin, dalteparin, tinzaparin and fondaparinux as one category.
A. I didn't know, but I'm not surprised.
Q. Because they're all the same pretty much; correct?
A. I think they're --
MR. COREY GORDON: Object to the form of the question.
A. -- in the same family.
Q. The same family.

Turning to page 73 of your report. Is page 73 the entire critique, in your report, of Dr. Jarvis?
A. Did I write anything else; is that what you're asking?
Q. Yes.
A. I think I don't have anything else in the report.
Q. And would --
And would you agree with me that the bottom of page 73 and 74 is your entire critique of Dr. Samet?
A. Yeah.
MR. COREY GORDON: Object to the form of the question.
Q. Now you would agree with me, doctor, that the majority of the articles that you cite deal more with superficial surgical-site infections and not periprosthetic joint infections.
A. Yeah. I haven't counted them up, but many of them deal with su -- with the superficial infections.
Q. And even though they're both infections, there is some difference in the mechanism of cause.
A. I'm not sure that's correct. In other words, my own concept is the initiation of infection

is quite similar. You have an or -- an organism that's part of the flora; to me that's the origin in both. The organism gets to the wound; that's the same. And it's there at -- usually at the time of incision.

After that, as I said, once the organism gets on the vascular prosthetic device it begins to go through some changes through quorum sensing, it does build up the biofilm, and that's different, vastly different.

Q. I understand that.

But you agree one of the differences is the quantity of bacteria required to cause the infection.

A. I think it's fewer bacteria to cause an infection with the prosthesis.

Q. And -- And one of the reasons is because when you have, for example, prophylactic antibiotics as well as the host immune system, that's much more effective at eliminating or attacking the bacteria than on a device that has no vascularity and therefore the host can't fight it off; correct?

MR. COREY GORDON: Objection, asked and answered.

A. Yeah, the way that I would -- yeah, I would say if you can't control the microbiome you're going

to get infections.

Q. Let's go to page 3.

A. Okay. Yeah.

Q. The chart you have on page 3, Figure 1, is right out of the 1996 Kurz study; correct?

A. Yes.

Q. Okay. You would agree with me that the first hour that a patient's being warmed the patient still becomes hypothermic in colorectal surgeries.

A. I think that's --

You know, if you ask what proportion of the time, I don't know, but they are hypothermic for awhile.

Q. Okay. Even with forced-air warming.

A. Umm-hmm.

Q. Is that a "yes"?

A. Yes.

Q. Okay.

A. Sorry.

Q. And you recall Dr. Kurz, in her deposition, discussing the types of infections that they were counting with respect to -- to calculate the incident of infection with forced-air warming and without forced-air warming. Do you recall that testimony?

A. No, --

MR. COREY GORDON: Object to the form of the question.

A. -- I don't remember that.

Q. Do you recall her stating that many of the infections that they were identifying were non-clinically significant infections?

MR. COREY GORDON: Object to the form of the question, mischaracterizes --

A. I don't remember that, --

MR. COREY GORDON: -- the evidence.

A. -- but I'd be happy to look at it again.

Q. You would defer to Dr. Kurz with respect to the interpretation of her own study; correct?

MR. COREY GORDON: Object to the form of the question.

A. Yeah. You know, we talked about this earlier where she changed her opinion, you know, through the start, so, but I -- yeah, in general she called that -- whatever she called the infection I would defer to her.

Q. Okay. Just like when you have a question about a study, you call the author of the study and ask questions; correct?

A. I do sometimes.

Q. Like you did with Dr. Darouiche.

A. I do.

Q. Okay. And with Dr. Chen; correct?

A. Yes.

Q. Okay. Because for the most part the person that conducted the study knows more about the study that was -- that was done; correct?

A. That's true.

Q. Okay. Now with respect to the oxygenation issue and the benefits of oxygenation by using forced-air warming, none of those studies looked at periprosthetic joint infections; correct?

A. I think that's true.

Q. Okay. And you agree with me that when Andrea Kurz indicated in her deposition with respect to what would happen if you did the study now and it would be a 30 percent reduction, that was speculation, that was a hypothesis; correct?

A. That's what she said. That's all I know.

Q. There is no data to support that; correct?

A. No. She was saying this is what it would look like in her opinion.

Q. And that was a hypothesis; correct?

A. Correct.

Q. And there are many times that hypotheses are wrong; correct?

A. Sometimes that happens.
Q. And that's why you do the study; correct?
A. Yes.
Q. Okay. So you agree that she admits that the reduction of infection is going to be a lot less than threefold, and it's her hypothesis that if the study was done now it would be about 30 percent reduction for colorectal surgeries.
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. I mean, what I would say is, you know, that study done, what, 20 years ago or so, in the meantime a whole lot of other changes, we'll just mention Darouiche and the -- and the antiseptic. And one of the concepts that I think goes on as you look at more recent studies, which reflects on your question, is what's the modifiable, residual modifiable effect you can have when you start adding all things that cut down the infection rate. It's awful hard to show, when you're moving away from that, if you have three or four or five, you know, improvements in outcome, then you have less proportion of infections you can impact with a new process or a new product.
Am I making sense, or?
Q. Wel, yeah, you're making...

Let me ask you a question. If a patient only used warm blankets during a total hip or total knee arthroplasty, do you know whether or not the patient would become hypothermic?
A. No, I don't know that. I don't know what the --
Q. So --
A. -- data show.
Q. -- sitting here today, you don't know whether or not just using warm blankets is just as efficacious as the forced-air warming.
A. I thought there were studies that showed it didn't work as well. Can't cite them right now, but I have read that somewhere.
Q. You haven't --
Did you ever look at the Dr. Sessler study of 2015 that compared just blankets to forced-air warming?
A. No. I don't know that one.
Q. And in fact you're familiar with the study that looked at the data out of Hopkins that showed no reduction in periprosthetic joint infections between patients that had thermoregulation and patients that didn't have thermoregulation.
A. You're talking about the first study in

my -- in my chart of the cohorts?
Q. I'm not sure, but do you recall the Hopkins study that looked at the Hopkins data?
A. Yeah, I think -- Let me just -- I have that in the chart of cohorts that we just looked at. Here we go. So page 8.
What I'm asking you, I guess, is are you referring to the study number 1 at the top? Hopkins uses a WarmTouch forced-air warming, and that was a big study, you know, 46,000 plus, it's a cohort. Amazing low percent that got hypothermic.
Q. Is this the Brown study?
A. Forgot the name of the first author. But the lead author is -- was an anesthesiologist I think, the other ones who did that.
Q. This is the Scott study; correct?
A. I think it's the Scott study. That's right, yeah.
Q. Okay. And if you look at the Scott study --
Do you know what the SCIP protocols are?
A. Yeah. I have an idea, yeah.
Q. So for wound infection, the -- when a -- when the patients were not com -- SCIP non-compliant you had 3.6 percent of wound infection, and when they were SCIP compliant they had 3.8 percent wound

infection.
So how do you get an SSI of -- a risk ratio of .86 for wound infe -- for surgical-site infection?
A. I don't remember how I got that, but it was clearly not significant.
Q. Okay. So you agree with me that even current studies show that there is no benefit with forced-air warming with respect to surgical-site infections.
A. Especially current studies, because of all the management that has gone on beforehand to introduce controls of the residual proportion of infections that you can mod -- you know, modulate.
Q. So you would agree with Andrea Kurz, then, that in -- in today's world, okay, --
A. Umm-hmm?
Q. -- that there's no scientific evidence that indicates that forced-air warming reduces the incident of surgical-site infections.
A. No, I won't --
MR. COREY GORDON: Object to the form of the question, and misstates the evidence.
A. No, I won't agree with that.
What I'm saying is she was saying that, look, you know, going forward with all the changes

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going on we might only see 30 percent instead of 67 percent reduction. That's what I recall, and that's what I cited in my report.
Q. But you also cited Scott --
A. Yeah.
Q. -- that showed that patients that were SCIP non-compliant had a lower infection rate than patients that were SCIP compliant.
A. Well if you look at all infections, that was statistically significant, all -- all infections. The surgical site he couldn't show a difference.
Q. Okay. We're not looking at all infections here, doctor.
A. Yeah, okay.
Q. We're looking at surgical-site infections.
A. Perfect.
Q. Which is a wound infection; correct?
A. Yes.
Q. Okay. And in the Scott study SCIP non-compliant had a lower infection rate than SCIP compliant; correct?
A. You mean a non -- nonsignificant --
Q. It's nonsignificant, but it was still -- it was still lower.
A. Fine.

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Q. Okay. I mean, you're right, it is nonsignificant --
A. Yeah.
Q. -- because the p value's .7811.
A. Yeah. Not at all.
Q. The p value's very high.
A. Yeah.
Q. So that would indicate to a scientist, such as yourself, that there's no difference between -- between warming and non-warming.
A. True.
Q. Okay.
MR. COREY GORDON: Object to the form of the question.
Q. Now you spent a considerable amount of time going over comorbidities.
A. Yeah.
Q. Okay. Can we just agree that the comorbidities will be case specific depending on the patient?
MR. COREY GORDON: Object to the form of the question.
A. So if you're asking can I predict the infection rate above or below the average as a result of incorporating comorbidities, yes. Is that what you're asking?
Q. I mean, for example, you talk about diabetes and obesity, --
A. Yeah.
Q. -- other things.
But you would agree with me that that discussion might be more appropriate when we actually know what patient we're talking about; correct?
MR. COREY GORDON: Object to the form of the question.
MR. ASSAAD: Basis?
MR. COREY GORDON: Appropriate to what? Appropriate to his discussion of why McGovern is not effective? No. The word "appropriate" is -- is completely vague and meaningless.
MR. ASSAAD: Why are you yelling to me, Corey?
MR. COREY GORDON: I'm not yelling. I'm -- You're detecting an exasperated tone in my voice, but I'm not yelling.
MR. ASSAAD: Are you picking up that stick to hit me?
MR. COREY GORDON: Not yet.
(Laughter.)
MR. GOSS: Let me tell you, it hurts when

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that thing comes down.
(Laughter.)
BY MR. ASSAAD:
Q. Are you aware of articles that discuss that the incidence of periprosthetic joint infections are going to increase over the next twenty -- up to 2030?
MR. COREY GORDON: Object to the form of the question.
A. Yeah, related to the increased number of people who are undergoing the procedures, so.
Q. When we talk about incidence, I'm talking about the percentage.
A. Percent?
Q. Do you recall an article that indicated by 2030 the -- the incident of periprosthetic joint infections will be as high as 6 percent?
A. I'm not aware of that at all.
Q. You would agree with me that being diabetic is not a cause of the infection.
MR. COREY GORDON: Object to the form of the question.
A. I don't agree with that at all. My view of infections, surgical-site infections is that they're multifactorial and the comorbidities, for example, are a -- one factor that can certainly change the baseline

rate if you're not having those comorbidities. So I look at all the risk factors as, if you will, risk factors and causes. So if you said to me, I have twins, one of them is -- you know, exactly the same genetics, same surgeon, same operation, everything the same except one's an obese diabetic, and that patient gets an infection post-op, of course the diabetes and the obesity contributed to that person's increased risk of infection.

Q. Doesn't that go to susceptibility?

A. What I know it goes to is -- at least in terms of diabetes and obesity, is a change in the microbiome. Is that what you mean by "susceptibility"?

Q. So you think in that -- And -- Okay.

I want to make sure I understand you. You think obesity and diabetes has an effect on the human microbiome.

A. It does, and I've cite -- several studies that I've cited.

Q. Okay. And therefore what type of effect; does it increase the -- the number of bacteria on the skin?

MR. COREY GORDON: Object to the form of the question.

A. Increases for sure the number of people who are nasal carriers of Staph aureus, and by definition those people are more susceptible to infections. There may be other things as well, but that's -- the study of the microbiome is pretty young still, but it's a remarkable thing that we have several studies showing that.

Q. But you still -- you agree with me that the fact that --

You still need the bacteria to cause the infection; correct?

A. Bacteria are necessary, not sufficient.

Q. You can't have an infection without the bacteria; correct?

A. That's true.

Q. Okay. And you are just saying that a person that is obese might be more likely to be a Staph aureus carrier or an MRS carrier.

A. That's for sure, and I know that person's at higher risk when you look at the epidemiologic studies, which I've cited, for getting a surgical-site infection.

Q. I understand that.

But my point is that makes them more susceptible, not that -- I mean --

The only thing I know that causes a periprosthetic joint infection is a bacteria; correct?

A. That's always there.

Q. Okay. The fact that I am -- someone's obese is not going to spontaneously have an infection without a bacteria; correct?

A. Correct.

Q. Okay. It is the bacteria that causes the infection, and it is the host that may be susceptible more or less than the average human and may allow the infection to progress.

MR. COREY GORDON: Object to the form of the question.

A. You and I are going to disagree. I mean, I think that risk factors are, by definition, causal, and -- that's why I tried to give you the twins, one was a diabetic obese, and without that that person, the twin, didn't get an infection. You're asking a little bit about mechanisms, which aren't fully worked out.

Q. Well the one that's diabetic obese compared to the regular twin, okay, the diabetic obese still would have to have a bacteria that would get into the joint area during the operation to cause an infection; correct?

A. Yeah. I mean --

Q. And the same thing with a person that's skinny; correct?

A. That's correct.

Q. Unless, let's assume it's the same amount of bacteria, say it's a thousand CFUs or 10,000 CFUs, okay? My understanding, and see if we could agree, that the diabetic obese patient is more prone to -- for the -- for the CFUs to -- to -- like -- more likely to become infected because that person is obese and a diabetic as compared to the healthy person.

MR. COREY GORDON: Object to the form.

Q. Do you understand what I'm saying?

A. Not really, no.

Q. Okay. You still need the bacteria to land on the -- the diabetic and obese person; correct?

A. Correct.

Q. If no bacteria lands on the joint during the operation of a diabetic obese patient, that patient, more likely than not, is not going to have an infection; correct?

A. Yes.

MR. COREY GORDON: Object to the form of the question.

Q. Correct?

A. Yes.
Q. And in fact it would be impossible, without bacteria, for that person to have an infection; correct?
A. Need the bacteria.
Q. Huh?
A. Need the bacteria.
Q. You need the bacteria.
Whether or not you are obese, diabetic, immunosuppressed and whatever type of comorbidity there is, you need the bacteria.
A. Yes.
Q. Okay. You could be immunosuppressed and go through a total hip and total knee arthroplasty, and as long as no bacteria lands in the joint area you're not going to get an infection; correct?
A. I think that's true.
Q. Same thing with a diabetic; correct?
A. Yes.
Q. Same thing with an obese person; correct?
A. Yes.
Q. Okay. You need the bacteria to get to the joint; correct?
A. You do.
Q. Okay. Go to page 13.

A. Sure.
Q. On the third paragraph from the bottom where it says: "Thus, substantial rises in comorbidities"? Do you see that?
A. I do.
Q. Okay. The last sentence you say, "...it has been reported that surgical site infection rates have fallen over time during the use of Bair Hugger." Correct? I read that correctly?
A. Yeah.
Q. You're talking about superficial wound infections; correct?
A. They're probably mixed.
Q. Well we just said there was no study on periprosthetic joint infections.
MR. COREY GORDON: Object to the form of the question.
A. Yeah. I don't know that they didn't count -- I mean CDC has rates for hips and --
(Interruption by the reporter.)
A. -- has rates of infection for total hip placement, total knee replacement from their national cohort. And what I cited in the report was if you look at the trends over time, and they corrected for some of the comorbidities the best they could, they've

actually shown a decline, something like 27 to 43 percent depending on one's hips, one's knees.
Q. Are you aware of the -- the Parvizi studies regarding the economic burden of periprosthetic joint infections?
A. I think so. I don't remember exactly what number he came up with, but.
Q. Well you know that Dr. Parvizi has looked at this issue; correct?
A. Yeah.
MR. COREY GORDON: Object to the form of the question.
MR. ASSAAD: Basis?
MR. COREY GORDON: What is "this issue"? You've just -- You've had a whole line of questions where you're asking him about the trends, and then you switch gears and then you say he's -- Parvizi has looked at "this issue."
BY MR. ASSAAD:
Q. Doctor, you knew what I was talking about when I said "this issue"; correct?
A. I did.
MR. COREY GORDON: Object to the form of the question, lack of foundation.
Q. We were talking about infection rates;

correct?
A. Yes.
Q. And Dr. Parvizi has looked at infection rates over time.
A. And he showed, yeah, a fall.
Q. You believe he saw -- he's seen a fall?
A. That's what he said.
Q. When did he say this?
A. In a paper.
Q. Okay.
A. Can we pull it out?
Q. Are you familiar with a paper titled Economic Burden of Periprosthetic Joint Infections in the United States, authored by Steven Kurtz, Evan Lau, Heather Watson, Jordan Schmier and Javad Parvizi?
A. I don't think I -- I don't remember it. That's -- I may have read it, I don't remember.
Q. Published in 2011?
A. Yeah, I don't remember it.
Q. I'm sorry. 2012.
A. I don't remember it.
Q. What Parvizi article are you referring to that says he reduced -- reduction of infection?
A. Let me see if I can find it. (Witness reviewing exhibit.) Oh, I was thinking -- it's the

Rasouli paper, but I was thinking he was a co-author.
Q. What page are you looking at, sir?
A. So page 13.
Q. What paragraph?
A. It's Roman numeral vi. And if Parvizi wasn't part of that study then that's my mistake, but Rasouli is actually the first author.
Q. Mohammad Rasouli?
A. I think that's right.
Q. Okay. Did you look at what ICD-9 codes they looked at in formulating this opinion?
A. I saw them, but I don't memorize those or anything, yeah.
Q. Okay. You could look them up, though; correct?
A. I could have, yeah.
Q. Okay. And you didn't do that in this case; correct?
A. No.
Q. Okay. And if you look at --
What do you think the infection rate is for primary total hip or total knee infections in the United States currently?
A. Currently?
Q. Uh-huh.

A. My estimate is probably one percent or so.
Q. Okay. So if that's the case, and I think that might be acceptable, Rasouli is only showing .2 percent infection rates for primary hip or primary knee. That sounds very low; doesn't it?
A. It does seem --
MR. COREY GORDON: Object to the form of the question.
Q. That seems very low, doesn't it, sir?
A. It seems low.
Q. Okay. Would that cause you any concern to see what -- to check to see how he calculated his infection rate?
A. It's one paper.
Q. Okay. And there's two papers by Dr. Parvizi that you have not looked at; correct?
MR. COREY GORDON: Object to the form of the question.
A. Don't remember which ones I didn't look at. Are they the ones you were talking about earlier?
Q. Yes.
A. Yeah.
Q. The economic burden ones.
A. Yeah, I don't remember that.
Q. Okay. You also have an opinion that the

number of health professionals in an operating room had no significant influence on bacterial counts in the operating room; correct?
A. What page you looking at?
Q. 16.
A. Sixteen?
Q. Yeah.
A. Under "Summary"?
Q. I'm sorry. I'm looking at something else. I apologize. Withdraw the question.
Okay. Let's go to page 19.
A. Yeah.
Q. This talks about your hierarchy of Bair Hugger studies; correct?
A. Sure.
Q. Okay. Can we agree, with respect to whether or not the Bair Hugger increases the bacterial load over the surgical site, that the Melling article is irrelevant?
MR. COREY GORDON: Object to the form of the question.
A. No, I don't know that I would agree. I mean, it adds data.
Q. Well the Bair Hugger's u -- we're talking about the Bair Hugger being used perioperatively;

correct?
A. Yeah.
Q. And the Melling was pre-warming; correct?
A. That's correct.
Q. So whether or not -- I mean we're not looking at pre-warming here, we're looking at perioperative warming. You understand that; correct?
A. I do, and I've cited the paper that says warming and pre-warming might last up to a couple of hours.
Q. But we're talking about --
Do you understand plaintiffs' allegations that the Bair Hugger increases the bacterial load over the surgical site?
A. What I remember that you asked me the hypothesis that I thought they had was that it created a kind of a dust storm from the floor that came up over the surgical site, yes.
Q. Well let's -- Yeah. So -- So there has to be a surgical site; correct?
A. Yeah.
Q. Okay. There's no surgical site or wound during pre-warming; correct?
A. That's true.
Q. So with respect to whether or not the Bair

Hugger increases the risk of surgical-site infection, you have to look at studies that deal with the Bair Hugger being used during perioperative warming; correct?
A. What I would say is if you have pre-warming and the body stays warm and you avoid all the vasoconstriction that cooling does, that's a good thing. Is that -- So maybe I'm not getting close enough here.
Q. Well plaintiffs' allegation for -- just keep it simple. The Bair Hugger is being used and it causes increased bacteria over the wound.
A. Umm-hmm.
Q. Okay? You understand that.
A. Yeah.
Q. Okay. Melling doesn't deal with perioperative warming; correct?
A. He deals with pre-warming.
Q. Okay. So that's a different situation of what plaintiffs' allegations are in this case.
A. Might be technically. I was just trying to say that the physiology is the same, that's all.
Q. Have you looked at the stu -- all the studies under the Biological Plausibility Studies on page 20?

A. Yeah. I have a table on that somewhere that might make it easier. Maybe it was earlier. (Witness reviewing exhibit.) Here we go.
Q. On page 14?
A. Page 14 and 15, yeah.
MR. COREY GORDON: 14 to 15, partly. Oguz isn't in that table, you discuss that elsewhere.
MR. ASSAAD: Do you want to testify some more, Mr. -- Mr. Gordon?
MR. COREY GORDON: I'm just trying to --
Q. So doctor -- doctor --
MR. COREY GORDON: Go back to 20 and have him talk about it from there rather than the table.
BY MR. ASSAAD:
Q. Doctor, do you know what device was used in the Zink study, which Bair Hugger device?
A. I don't -- No. Don't remember.
Q. So you don't know what -- what the airflow of that device was?
A. No.
Q. Okay. Don't you think it'd be relevant to determine whether that study applies to the device that's being used in this litiga -- being -- in this litigation?
A. Told you I don't know what device they had

there.
Q. That wasn't my question, sir.
A. Yeah.
Q. Don't you think knowing what device was studied is relevant to determine whether that article is relevant to the device that's being used in this litigation?
A. Could --
MR. COREY GORDON: Object to the form of the question.
A. Yeah, it might be. I don't know.
Q. It may be; right?
A. Yeah. Yeah. Might be.
Q. And you don't know today what device was used; do you?
A. Yeah, I don't.
Q. Okay. The Hall -- The Hall is a poster; correct? A.C. Hall?
A. It was.
Q. It's not peer reviewed; correct?
A. I'm not sure it wasn't peer reviewed, but it wasn't a peer-reviewed full article.
Q. Okay. Well --
(Interruption by the reporter.)
Q. And that was in 1991; correct? December 9th

--
A. Yes. Yes, yes.
Q. Do you know what device was used in that article?
A. No, I don't.
Q. Okay. So it might be a different device that is at issue in this litigation; correct?
A. I don't know. Might be.
Q. Okay. And that would be relevant.
A. Might be.
Q. Okay. The Huang article, do you know what device was used in that case?
A. No.
Q. And do you have any criticisms of these articles?
A. They're small studies, they're not always, you know, controlled studies. Well they are, I guess. Well one of them wasn't, the Dirkes study. But mostly I think they're just small studies that try to look at, I think, a relevant question.
Q. By the way, does it -- do you take into consideration who funds the studies?
A. You have to look at that.
Q. Okay. But just because a person funds a study doesn't mean the study's not a good study;

correct?
A. I would say that's true.
Q. Okay. Otherwise, I mean, you would eliminate most of the studies that are out there because they're usually financed by a corporation.
A. Well I've done a lot of studies funded by industry, and as I told you, many of them turn out to be nothing, and I wrote the paper up and kind of read 'em and weep.
Q. And usually good studies -- or corporations, when they fund a study, should not be involved in the study; correct?
A. Yeah. When I've done studies myself, they haven't been involved.
Q. They should have no editorial review of the studies.
A. Actually, as a courtesy after each of those studies, most of us would give industry some time period, like 30 days to look at it. They can make comments, but we make the final decision.
Q. Okay. But you wouldn't give them carte blanche to make any changes to the --
A. Oh, no.
Q. Okay. That would be unethical; wouldn't it?
A. That'd be --

Yes.
Q. Okay. I mean, look at the Zink study. That only had eight volunteers; correct?
A. That's true.
Q. That's a very small study; correct?
A. That's true.
Q. Okay. If -- When we're looking at bacterial load with airborne contamination, that is a very underpowered study; correct?
A. It's under --
MR. COREY GORDON: Object to the form of the question.
Q. Very underpowered; correct?
A. It's underpowered.
Q. Okay. And in fact do you know whether or not -- I mean, you agree with me, as we stated before, that the amount of people in the operating room have an effect on the bacterial load in the operating room; correct?
A. I think they do.
Q. Okay. Do you know how many people were in the operating room when they did this study?
A. Don't remember, no.
Q. Okay. Because it would be a big difference if there was only one person, the patient, as compared

to the patient and six or seven or eight people in the operating room; correct?
A. I think there would be a difference.
Q. Okay. And when you do a study you want to imitate the study as much as possible to what really happens in real life; correct?
A. Yeah, always. Yeah.
Q. Okay. Otherwise, I mean, you might get results, but it's hard to apply those -- the results to make decisions with respect to clinical care if the scenarios are not similar; correct?
A. It's easier to make results if you have a -- the closer it is to what goes on, no question. But I wouldn't throw the studies out, if that's part of the question.
Q. Well I don't see you criticizing any of these studies in here that's saying that they're underpowered.
A. I didn't say that. I just told you they're underpowered and they're small studies.
Q. I understand. And you criticized McGovern and you criticized all these other studies, but you don't criticize the studies that 3M relies upon.
MR. COREY GORDON: Object --
Q. Why is that, sir?

MR. COREY GORDON: Object to the form of the question.
Q. Why is that, sir?
MR. COREY GORDON: Object to the form of the question.
A. I'm very happy to talk about this, you know, but.
Q. We can talk about it all you want, but I'm saying why in your report you did not criticize or discuss any of the weaknesses in the studies that 3M rely upon.
MR. COREY GORDON: Object to the form of the question.
A. Yeah, I -- I think I took these studies, this is what I found, and collectively they showed nothing in terms of colony-forming units increasing as a result of the Bair Hugger.
Q. But you would criticize Zink, Hall, Huang, Dirkes, and Moretti as being underpowered, wouldn't you?
A. So these are small studies, that's true. That's the best data we have.
Q. Did you criticize them at all and say they're underpowered in the paper?
A. I didn't do that.

Q. That's not being objective, sir, is it?
A. I think I --
MR. COREY GORDON: Object to the form of the question.
Q. That's not being objective, sir, is it?
A. I think I'm fine with this.
Q. Oh, you're fine with that, okay.
A. Yeah.
Q. That wasn't my question.
Is that being objective?
MR. COREY GORDON: Object to the form of the question. Move to strike counsel's snide comment.
Q. You cite Avidan; correct?
A. Yes. On the next page, 15.
Q. That was a small study as well; correct?
A. It was a small study.
Q. Okay. And you don't know what device was used in that case; do you?
A. No, I don't.
Q. And Occhipinti, you don't know what device was used in that case; correct?
A. Don't know what device.
Q. And that dealt with surgical drapes; correct?

A. It's what?
Q. That dealt with surgical drapes.
A. Yes.
Q. Okay. Did you read the letter to the editor by Farhad Memarzadeh in the Moretti case?
A. No.
Q. Any criticism of Avidan besides it's -- it's a small study?
A. Well, I mean, one of the things you would say is when the plates were directly in the airstream 16 be -- inches below the end of the hose you could argue that you're not really sure what was coming out was from only the hose or the air below. That would be one criticism.
Q. Okay. You didn't put that in your report; did you?
A. No, I didn't.
Q. Okay. You cite to the Oguz study; correct? O-G-U-Z.
A. Yes. Yes.
Q. Any criticism of that study?
A. It was pretty good. He randomized people, there were 80 orthopedic patients, and he looked at the influence of either device on the CFUs and found none.

Q. "Found none"?
A. Huh?
Q. "Found none"?
A. No influence.
Q. So you wouldn't agree with me that if you looked at the comparison between the Bair Hugger and the HotDog in the Oguz study that there was an increase in bacterial load using the Bair Hugger over the HotDog?
MR. COREY GORDON: Object to the form of the question, mischaracterizes the evidence.
A. I mean, what he found at the end using his model, multivariate model, and asked the question, does the individual device actually influence the counts, and he couldn't find it.
(Wenzel Exhibit 11 marked for identification.)
BY MR. ASSAAD:
Q. What's been marked as Exhibit 11 is the Oguz article --
What's been marked as Exhibit 11 is the Oguz article that was provided to us by Dr. Wenzel today, August 4, 2017, according to a subpoena that was issued to be produced to us by June 21st, but we got it today.

And it's underlined by Dr. Oguz; is that correct?
A. Underlined by me?
Q. Yes.
A. Yeah.
Q. Okay. Can I have that back, please?
A. Sure. (Handing.)
Q. Now what you didn't underline here was the statement by the authors that, this study may obviously not be generalized for an overall safety statement on forced-air warming, and is primarily applicable in the particular surgical setup.
You didn't underline that; did you?
A. No.
Q. Okay. That's a pretty important statement by the authors; isn't it?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. Where am I looking here?
Q. (Indicating.) Right after you stopped underlining up here.
A. Right there? (Witness reviewing exhibit.) So you're saying "only the maximum number of health professionals" --
Q. No. Over here, sir. Right after this

underline here. [Indicating.]
A. Oh, this one. Okay. (Witness reviewing exhibit.)
It might not. So I think that -- I think good authors will try to look and give their own critique of potential shortcomings.
Q. Okay. Now let's look at the table underneath there that looked at the multivariate analysis.
Do you agree with me for four out of the six plates that there is a higher incident of bacteria when forced-air warming was used as compared to when forced-air warming was not used, or when the HotDog was used?
A. Where is this?
Q. Table 2.
A. Oh, I'm sorry. It's these?
Q. Yeah. The second line down.
A. Okay. (Witness reviewing exhibit.) So what are you -- Make sure that I know what you're looking -- what numbers.
Q. Let me read it out loud for you.
A. Yeah. Go ahead.
Q. Table 2 is the results of a multivariate analysis of factors; correct?

A. Yeah. Yeah.
Q. And that's what you were talking about; correct?
A. I am.
Q. And it looked at the presence of forced-air warming; right? On plate 1 it was 1.13; on plate 2 it was 1.07, and you even highlighted it in blue; plate 3 is 1.30; plate 4 is 1.55; and plate 5 and 6 are 1.0. Is that correct?
A. Let me look. In the "absence of laminar flow," you're looking at that, or the "presence of forced air warming"?
Q. "Presence of forced air warming."
A. Yeah, that's correct.
Q. So with the presence of forced-air warming there was an increase in bacterial load over the surgical site.
MR. COREY GORDON: Object to the form of the question.
Q. That's what those numbers mean; correct? For four out of the six plates.
A. Oh, I see what you're saying. Yes.
Q. Okay.
A. For four out of the six, yeah.
Q. Okay. And you are aware that the -- only

one surgery dealt with total knee replacement.
A. I think that's right.
Q. Okay. Most of them were short surgeries; correct?
A. Yes.
MR. COREY GORDON: Object to the form of the question.
Q. Let's move on to page --
Go to page 34 [Exhibit 1].
(Discussion off the stenographic record.)
MR. ASSAAD: Let's take a break then.
(Recess taken from 3:53 to 4:02 p.m.)
BY MR. ASSAAD:
Q. Ready to continue, doctor?
A. Sure.
Q. Now let's look at page 34.
A. Okay.
Q. You go over three studies that talk about the nasal colonization of Staph aureus?
A. Yeah.
Q. You agree with me that none of those studies looked at the incidence of periprosthetic joint infection; correct?
A. Let me see where I am here. (Witness reviewing exhibit.) You're sure Kalmeijer? I just

can't remember exactly.
Do you have that paper, just remind me.
Q. I do have Kalmeijer, I only have one copy. You don't have it with you?
A. No. I don't have anything.
Q. Okay. Well actually, let's look --
MR. COREY GORDON: He might in the box, if not what's up there.
A. Yeah, I don't know.
Q. Let's look at Kalmeijer, which is the surgical site in -- you can use my copy -- surgical-site infections in orthopedic surgeries.
Is that the paper you're referring to?
A. Yeah.
Q. Okay.
A. Is it -- If it's not joints, I just wanted to make sure. I thought it included --
Q. Actually, if you look at the page that looks at the number of patients, --
A. Yeah?
Q. -- you can see that in -- when mupirocin is used --
A. Mupirocin, right.
Q. -- there were zero infections; correct?
A. Yeah.

Q. And then when the placebo is used there was only one infection; correct?
A. Yes.
Q. That's not --
A. Deep infection.
Q. Yeah. And we're talking about deep infections; correct?
A. Yes.
Q. That's not statistically significant; is it?
A. I don't think so.
Q. Okay. So would it be fair to say that if you used --
Is it mupirocin?
A. Mupirocin, yeah.
Q. -- mupirocin, that there is no data that indicates that it would statistically impact deep joint infections?
A. In that study.
Q. In that study, okay.
And you consider this study authoritative; correct?
A. Yes.
Q. Okay. What about the other studies? Do you agree with me that none of them found that nasal -- nasal colonization of Staph -- of Staphylococcus had

any effect on periprosthetic joint infection?
A. Well I showed you the data from Chen, and in the articles I even had the graph, I think, related to that.
Q. I'm talking about page --
A. They were mixed --
Q. Okay.
A. -- deep and superficial, but they were prosthetic joints.
Q. Those were the types of surgeries; correct?
A. Yeah. Is that what you want?
Q. No. But the difference is whether or not it caused a superficial wound infection or a periprosthetic joint infection. And there's no data that having colonization of Staph in your nose has an effect on periprosthetic joint infection; correct?
A. Yeah, I -- Again, Chen. Let's look at that, because I thought --
Where do I have that in my notes? He has --
Q. What page are you referring to?
A. Well I'm trying to find it. Maybe it was earlier. (Witness reviewing exhibit.) Sorry I'm taking so long.
Q. Why don't you look at page 65?
A. 65?

Q. You talk about Chen, et al, Clinical Orthopedic?
A. Yeah.
Q. Yeah. Page 65.
A. No, that's not right; is it?
Q. I'm sorry. Sixty-four.
A. Yeah, that's right. Okay. Thank you.
So, let's see. (Witness reviewing exhibit.) What I remember that the study said is they mixed superficial and deep in their review of the literature because it wasn't always clear. So it might be a mix of some of these.
Q. So sitting here today there is no evidence or data that indicates having colonization of Staph in your nose significantly increases the risk of periprosthetic joint infection; correct?
MR. COREY GORDON: Object to the question, mischaracterizes his testimony.
A. Well what I said is there's a mix of -- of periprosthetic joint infections and the more superficial ones in here, and I can't tell you, you know, what proportion.
Q. Okay. So you have no opinion. You can't make the statement today --
A. Oh, I make an opinion, yeah. I mean I would

-- You're going to surgery? Yeah, I'm going to tell you before you take your hip get the mupirocin.
Q. I understand that.
A. That's my opinion.
Q. There's no data that --
I mean the only study that we have that compared the two between a deep joint using --
A. Mupirocin.
Q. -- mupirocin and not is the Kalmeijer study; correct?
MR. COREY GORDON: Object to the form of the question, mischaracterizes his testimony.
A. Other -- What I just said, there's a mixture here. I can't take out pure prosthetic joint infections. Is that what you mean? Then I don't have that. It's a mixture of periprosthetic joint infections and the superficial ones, and she has five studies here and they all show 50 percent reduction or more.
Q. But they -- they might be a 50 percent reduction in just superficial wound infections; correct?
A. I don't think there were zero prosthetic joint infections in these the way that article was.
Q. Can you --

I mean, if you wanted to do a study to look at whether or not mupirocin reduces the incident of periprosthetic joint infections, you have to look at just periprosthetic joint infections; correct?
A. That's ideal, right.
Q. Okay. And one study we are aware of looked at that, and that is the Kalmeijer study that you consider authoritative; correct?
A. Yeah.
Q. Okay. And they saw no difference between using mupirocin and not with respect to deep joint infections; correct?
A. That's what they showed.
Q. And as of right now that is the only data that we have available with respect to deep joint infections. Solely on deep joint infections, not combining everything together.
A. When you say it that way, "solely," yes.
Q. Okay. Because when you start looking at superficial wound infections then you really have to look at, you know, you really can't make a -- a -- a reliable opinion with respect to periprosthetic joint infections because for -- it could be possible that you're looking at just a reduction in superficial wound infections; correct?

MR. COREY GORDON: Object to the form of the question.
A. Hypothetically, according to that, yeah. I mean, it's --
Q. Okay. All right.
Now you agree -- Let's look at page 38.
A. Yeah.
Q. Okay. This is your discussion on your opinions on laminar flow and rates of SSI; correct?
A. That's true.
Q. And Lidwell, the Lidwell studies were done in the '80s; correct?
A. That's right.
Q. And then the Brandt study was done in -- recently; correct? 2008?
A. 2008 I have the publication.
Q. Okay. And Gastmeier's 2012; correct?
A. Gastmeier's two thou -- Yes.
Q. Okay. Now you would agree with me that during the time that Lidwell was doing his -- his studies, that the -- that the Bair Hugger wasn't used in the operating room; correct?
A. Yeah, pretty sure it was not.
Q. Okay. But in the Brandt study and the Gastmeier study you agree with me that the Bair Hugger

was used or could have been used in the operating room; correct?
A. I would say "could have." I don't know. I don't remember.
Q. Well based on your education, training and experience, and your understanding of the use of the Bair Hugger, can we agree that more likely than not that the Bair Hugger was used --
A. I think it was --
MR. COREY GORDON: Object to the form of the question, lack of foundation.
MR. ASSAAD: I didn't finish my question. Can you please wait for me to finish my question?
MR. COREY GORDON: Sure.
Q. Based on your education, training and experience, and your understanding of the Bair Hugger and its use during operations, that more likely than not that the Bair Hugger was used in the surgeries that Brandt and Gastmeier reviewed?
MR. COREY GORDON: Object to the form of the question, also lack of foundation.
A. So two thou -- The Bair Hugger's been in, let's say 25, 30 years, so I would have thought so, but again, I don't know.
Q. Okay. Are you aware that 3M admits that

every study that looked at whether or not the Bair Hugger increased particles or hydrogen bubbles over the -- Sorry. Strike that.
Are you aware that Bair -- 3M admits that every study indicates that whether you looked at hydrogen or particles, that both were increased when the Bair Hugger was turned on as compared to the Bair Hugger was turned off?
MR. COREY GORDON: Object to the form of the question, misstates the evidence.
A. So I'm not aware that 3M admitted that. No, I'm not aware of that.
Q. If that is the case, would that cause you any concern that the Bair Hugger increases particles over the surgical site?
A. What I know now it would cause me no concern because all the studies that get closer, looking at CFUs, can't show that.
Q. Well are you aware of the Stocks article that did a correlation between CFUs greater than 10 microns and --
A. Yes.
Q. -- and --
A. I'm sorry.
Q. -- and CFUs?

A. Yes.
Q. Do you agree with that study?
A. Yes.
Q. Okay. Page 46.
I just want to understand your CDC NNIS score.
A. Yeah.
Q. And I guess you look -- to determine the risk factor for a surgical site risk, one of the things you can look at is an NNIS score; correct?
A. Yes.
Q. Okay. And when you talk about the surgical-site infection risk, do you know whether or not the CDC is referring to a superficial wound infection or a periprosthetic joint infection?
A. I don't know for sure.
Q. Well that would be --
Since we're talking about, in this case, periprosthetic joint infections, that would be relevant; correct?
A. Yeah.
Q. Okay. Now if you look at the criteria --
Well what's your understanding of the length of time of a -- a -- and I might have asked you this -- a length of time for a total hip or total

knee?
A. I think they're around two hours.
Q. Okay. So you agree with me that most likely the last criteria you offer one point for if op time exceeds the seventieth percentile for that procedure, or greater than three hours for a joint --
(Interruption by the reporter.)
Q. -- if op time exceeds the 75th percentile for that procedure, or greater than three hours for the joint replacement, that we could probably eliminate greater than three hours as one of the criteria that would be -- apply to total hip and total knee.
MR. COREY GORDON: Object to the form of the question, --
A. These --
MR. COREY GORDON: -- lack of foundation.
A. These are not my criteria, these are, you know, CDC's, and I don't think today there would be that many patients who would have more than three hours.
Q. Okay. And we could agree that for total hip and total knee it's not a contaminated or dirty surgery; correct?
A. Yes. It's a clean surgery.

Q. Okay. And the ASA score is based on the patient; correct?
A. It is.
Q. Okay. Now where it says, "if op time exceeds the 75th percentile for that procedure," is there somewhere I could look at to see what the -- the time for each type of procedure is?
A. I think there is, but I -- I don't know the CDC reference for that, though.
Q. Okay. Looking at the bottom, the odds ratio of the variables.
A. Yeah.
Q. Why is it if you have private insurance you're less likely to get a surgical-site infection?
A. My guess is that it's a surrogate for healthier people who are less likely to have some of the other comorbidities. I don't know the answer, but that's my thought.
Q. Go to page 49.
A. Okay.
Q. You write: "Of interest, there were no prosthetic joint infections...among diabetics who were not obese..."
Did I read that correctly?
A. You did.

Q. So would you agree with me that the mere fact that you have diabetes, that it does not increase the risk of periprosthetic joint infection?
A. No, I wouldn't. This is this study, and that's what I would cite to say in that study that's what they found.
Q. Okay. Well what's your opinion, sir?
A. I think diabetes is a risk factor.
Q. Okay. So you disagree with the --
A. I do.
Q. -- the results of the study.
A. I do.
Q. Okay. But you cited this study in your report.
A. Sure. I told you I'm trying to show you everything I have.
Q. And you would consider obese a BMI greater than 30; correct?
A. Yes.
Q. And you'd agree with me that there is a big difference with respect to risk factors of surgical-site infections between obese and morbidly obese.
A. Yeah, I think it's probably worse with morbid obesity, yeah.

Q. And I believe you cited an article you looked at where they looked at the BMI greater than 30 and the BMI greater than 40. Is that -- Am I recalling that correctly?
A. You may. I can't think it -- I don't know what that is right now, but it might be so.
Q. So I understand that you read many articles and did an extensive literature search with respect to formulating your opinions in this case; correct?
A. Yes.
Q. Okay. So when you come to your ultimate opinions, what methodology did you use in doing your review to determine your opinions?
A. What I think I've done is actually take a look at the hierarchy of all the studies that fell into any one group. So I looked separately at clinical trials, I looked at meta-analysis, case-control studies, cohorts, national trends, and then the data on CFUs as a biological plausibility. I have -- There are 15 studies from there. I looked at the particle studies, which I think are really distant surrogate markers of infection. And then together, I would say, as -- as a complete package, I can't find any, you know, convincing link between the Bair Hugger and harm.

We can talk about the McGovern study as the one sort of study that stands out until recently. They gave an initial signal, but the more I looked at that study, the more problems I had with it.
Q. With respect to your methodology to de -- Strike that.
We've talked about some studies today in which they offered data or opinions that contradict your opinions; correct?
A. There were some.
Q. Okay. What was your methodology to de -- in determining which studies you would use to support your opinions and which studies that you would disregard?
A. I don't know that I would sort of just blatantly disregard anything. I looked at the collective sort of sense within each category, if I could.
Q. Well, for example, you think that nasal colonization of Staph will have an effect on periprosthetic joint infection, but you disregard the only study that looks at it that says there is no statistically significant difference.
MR. COREY GORDON: Object to the form of the question, mischaracterizes his testimony.

A. I think the -- the bulk of data, so many different studies, including orthopedic studies where I gave you from Chen, there is no way that I would want the orthopedic patient not to have nasal mupirocin preoperatively, and that's pretty much the standard around the country.
Q. Well that's not the standard where Darouiche did his study; correct?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. Yeah, I -- I -- he -- that study, no. In terms of that study, he didn't do that, but --
Q. Okay. So --
A. -- that wasn't prosthetic joint infections. Are you talking about the first study?
Q. Yes.
A. Of the -- Using the antiseptic?
Q. Yeah.
A. Yeah, that's -- that's obviously different than prosthetic joints.
Q. So you would use it for prosthetic joints but not for other surgeries?
A. Yeah, there -- I -- I think the standards are today, any implant; so orthopedic implant, cardiac implant, and neurosurgery implant, all those people

should be getting mupirocin and chlorhe -- and chlorhexidine baths.
Q. And the mupirocin is for the nose; correct?
A. It is.
Q. Okay. So that would indicate to me that you are trying to kill the bacteria in the nose so it doesn't become aerosolized; correct?
MR. COREY GORDON: Object to the form of the question.
A. No, that's not the... I'm trying to kill the bacteria in the nose, and if you kill the bacteria in the nose you actually show a markedly reduced bacterial burden in the rest of the body.
Q. How does that occur?
A. You know, the joke that I use is think about all the people that touch their nose when they -- you know, during the day, and 30 to 50 percent of people who have Staph aureus in the nose have this on the strai -- on their hands, and when you do fingerprints, 97 percent are the exact same strain. So I don't know for sure, but I think that we all have a lot of contact with our nose and mouth.
Q. And when do you give the mupirocin to the patient?
A. Ideally you would have them come into the

pre-op center and -- where they get evaluated in general for anesthesia five days before the surgery, and then twice a day for five days.

Q. So I'm just trying to understand, like, when you look at a -- a peer-reviewed article, what methodology do you have to determine whether or not the article is something that you're going to rely upon and agree with as compared to something that you may not agree with?

A. Well I could go on for a long time, but I think what I would do is look at the methods section in a very critical way. For example: Did they have a clear hypothesis? Did they have a clear endpoint? If they're counting infections, what was the method of case finding? Was there any validity to the case finding technique? You know what I mean by that? When I say -- I'm going to go back. If they say they found it, was it really a case, or was it a mistake? Was it -- What kind of study was it really; a prospective, a clinical trial, was it observational trial? If it was observational, were the two things that we're interested in looked at concurrently? I'd want to know a little bit about how they, you know, did some power studies, what Alpha was in the study, and the length of follow-up, of course, would be all

important things. I'd want to look at what statistics that they used and how they were going to evaluate success or not. And I would hope that they would have not only efficacy, but a safety profile to go along by which you could make a, if you will, risk/benefit compared to an alternative.

I could go on for awhile, but I think you got the idea.

Q. I think I get the idea.

MR. ASSAAD: So let's mark this as the next exhibit.

(Wenzel Exhibit 12 marked for identification.)

(Discussion off the stenographic record.)

BY MR. ASSAAD:

Q. Do you --

Have you seen this article before?

A. I don't know. I'm not sure I have, but.

Q. I represent to you that it came out of the box of documents that you provided to us today.

A. Yeah. You know, when you read a lot, I'm not positive. I want to be able to tell you accurately.

Q. And if you look at a couple pages later, I think the next page, it's actually underlined in

certain areas.

A. Okay. (Witness reviewing exhibit.) Oh, in the "DISCUSSION." What do you want me to tell you?

Q. I mean, is that your underlining?

A. Oh yeah, it is.

Q. Can I look at it real quick, please?

A. Yeah, sure. (Handing.)

Q. You highlighted, in the --

And what Exhibit 12 is is the article titled Forced-Air Warming Does Not Worsen Air Quality in Laminar Flow Operating Rooms, authored by Dr. Sessler, Dr. Olmsted and Kuelpmann. Is that correct?

A. I think they're the authors, yeah. Yeah.

Q. Why wasn't this article, which is clearly something you reviewed, in -- somewhere in your report?

A. I don't know. Don't remember.

Q. Were you told by anyone not to include this article in your report?

A. First of all, no one's told me anything, and I wouldn't listen anyway.

Q. Okay. You underline, "Our results are consistent with computational fluid dynamic models that show that properly designed air handling systems combined with natural protective aspects of convective

currents up from the patient, are effective in reducing particle concentrations" near surgical -- "near the surgical site."

A. Yeah. That's what he said.

Q. Well my question is why did you underline that section?

A. You know, a lot of times I underline things because, one, I don't understand and I want to read it a second time, or I wanted to ask a question from counsel. And as I told you earlier, I'm one of these guys that often underlines, you know, a big chunk of the re -- if you gave me a novel, unfortunately, I'd ask you if you wanted it back because I underline that stuff.

Q. So sitting here today you don't know why you underlined it?

A. I don't remember.

Q. Okay. Now do you recall --

You said you've read the Sessler depositions; correct?

A. I think so. I don't remember a lot of -- I thought I had.

Q. Do you recall the discussion I had with Dr. Sessler during his deposition regarding his tests?

A. No, but go ahead. Remind me.

Q. You haven't seen the raw data for -- for --
You haven't seen the raw data for the -- for this study; correct?
A. Correct.
Q. Okay. Now just so I understand your opinion, if a device significantly increases particles over the surgical site is it your opinion that the -- there is going to be no effect on surgical-site infections?
MR. COREY GORDON: Object to the form of the question, also incomplete hypothetical.
A. You know, I hate to say "always" or "never," I've told you that today. So I'd hate to say "never, ever." But in general for me to think that particles are really important would be if that was linked directly in some way to surgical-site infections and not just be a surrogate marker.
Q. You agree with me that Stocks linked particles to bacteria for particles greater than 10 microns; correct?
A. He did. I agreed.
Q. And you agree that Darouiche linked CFUs to -- the -- the amount of CFUs to periprosthetic joint infections; correct?
MR. COREY GORDON: Object to the form of

the question.
A. Yeah. That was his link, yes.
Q. And you agree with that?
A. Yeah.
(Interruption by the reporter.)
A. His link, yeah.
Q. Okay. So if you're looking at just 10 micron particles, would you agree with me that an increase in 10 micron particles over the surgical site would increase the risk of periprosthetic joint infection?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.
A. That's the question that we're trying to get at, and I don't think we have conclusive information that particles equal infections.
Q. Are you looking for a hundred percent certainty?
A. I never look for a hundred percent, sir.
Q. Well do you remember back in, maybe it was high school, we had to learn logic? Remember that?
A. Yeah. I took a college, not high school course, in logic.
Q. Okay. You know, if you -- A -- you know, if A equals B and B equals C, then A could equal C?

A. I know what you're getting at.
Q. You remember that?
A. Yeah.
Q. Okay. So --
MR. COREY GORDON: Socrates was a man.
Q. So if -- if Stocks linked particles over 10 microns to bacterial load, and Darouiche linked bacterial load to periprosthetic joint infections, and I understand you have an issue with where is that bacteria coming from, but based on those two studies, and logic, do you not agree that if 10 micron particles increase over the surgical site there is going to be an increase in periprosthetic joint infections?
MR. COREY GORDON: Object to the form of the question, also lack of foundation, incomplete hypothetical.
A. Well I like the logic part, but if you're talking about Darouiche's study based on four infections, even he says we need to go back and get a much bigger study to see if this is real. That's my -- my recollection of what he did in the discussion.
No one's going to take that kind of study and make a blanket statement about all surgeries.

Q. But you, sitting here, cannot say that my statement is not true; correct?
A. I --
MR. COREY GORDON: Object to the form of the question.
A. I don't think it's true. I think it's -- we need a lot more information for your statement --
Q. Okay.
A. -- to be right, unless you're making it totally hypothetical.
Q. I didn't ask you if it was true.
You can't offer the opinion that that -- that that progression between Stocks and Darouiche and particles over 10 microns can be correlated to periprosthetic joint infections is not true.
MR. COREY GORDON: Object to the form of the question, --
Q. You just want more data.
MR. COREY GORDON: -- in --
Object to the form of the question, incomplete hypothetical.
A. Well I want more data, and also, you know, I'd say if you -- Well, let me pause for a second. I'm trying to -- I'm getting a little tired, I think.
Q. Let me withdraw the -- Let me make it a

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little bit easier, okay, because I know it's a lot of thinking.

For example, if Darouiche came out and came up with -- did the same exact study and showed no correlation between CFU load over the surgical site and periprosthetic joint infections, then there would be no need for a further study because that study indicated that it's irrelevant; correct?

A. If a --

MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.

A. If a new study came out, much bigger and showed there's nothing going on, yeah, I think that would be the end, or -- or certainly close.

Q. My point is, further study is needed; correct?

A. For sure.

Q. Okay. And the reason why you think further study is needed, because you can't exclude the fact -- the scenario that if you increase 10 micron particles over the surgical site it would have no effect on periprosthetic joint infections.

A. I've seen --

MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.

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A. -- just no data that I can say to answer that no, so that's right.

Q. But you can't exclude it either; can you?

A. I can never exclude things that aren't there.

Q. Okay. Especially after the Stocks and Darouiche study; correct?

A. Yeah.

Q. Okay.

A. I mean that's...

Q. Let's talk about heater-cooler.

A. About what?

Q. The heater-cooler.

A. Okay. Sure.

Q. And I believe that's on page 75.

A. Yeah.

Q. Now you understand that the heater-cooler device is not near the surgical table.

A. The device itself is away from the table, yeah.

Q. It's actually probably in the corner of the room.

A. Often far away, yeah.

Q. Okay. And it is -- it has tubes that carry water to either heat or cool down the patient; correct?

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A. Yes.

Q. Okay. And the water is --

It's a closed system; correct?

A. It's not so closed as -- as what I've heard from our perfusionist.

Oh, that part, the tubing is.

Q. Yeah.

A. Yeah, not the tank of water.

Q. Which is -- the tank --

A. I'm sorry.

Q. -- the tank's in the corner of the operating room; correct?

A. The tank is, yeah.

Q. Okay. But the --

A. And they have --

Q. -- tube is closed; correct?

A. -- tubes that -- tubes are closed.

Q. Okay. And it might not -- there might be some leaks or some vapor inside the -- the heater-cooler unit; correct?

MR. COREY GORDON: Object to the form of the question.

A. You're talking about above the tank of water?

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Q. Or -- Or inside the heater-cooler unit where the tank is, it might -- there might not be fully closed or there might be some leakage or vapor.

MR. COREY GORDON: Object to the form of the question, also lack of foundation.

Q. Let me ask you this. Why do you -- Why do you not think it's a closed system at the heater-cooler device?

A. Well, I mean, you just open up the thing a little bit, I had the perfusionist show me this when they started to have infections about a year and a half ago, and you can just see this big tank of water.

Q. Okay. And what do you see?

A. And there's a fan right behind it, yeah.

Q. Okay. And -- And you're saying the fan is blowing the water?

A. It's blowing above the water.

Q. Okay. And what does that cause?

A. Aerosol.

Q. Aerosol that could be contaminated?

A. This study they showed that the air contained Mycobacterium chimaera.

Q. Okay. And it actually reached the patient; correct?

(Interruption by the reporter.)

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Q. And it actually reached the patient; correct?
A. It did.
Q. And so it was an airborne contamination that caused the infection to the patient; correct?
A. Yes.
MR. COREY GORDON: It's actually "Mycobacterium chimaera."
THE REPORTER: Thank you.
Q. You do not dispute the fact that the Bair Hugger harbors bacteria, --
MR. COREY GORDON: Object --
Q. -- the device itself.
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical, lack -- lack of foundation.
A. So there've been some cultures of the tubing that have shown organisms, and some have been swabbed, some have been rinsed, I think, and I think I showed these in my report, everything that -- that I knew about that.
Q. So you don't dispute that the Bair Hugger is contaminated internally.
MR. COREY GORDON: Object to the form of the question.

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A. It -- In some studies they found bacteria. It's not sterile.
Q. Okay. And it can't be cleaned; correct?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. I've read that, but I don't know, I mean.
Q. Well you've seen the device; correct?
A. Yeah. I have.
Q. Are you aware of anyone that's ever cleaned the inside of the hose of a Bair Hugger?
MR. COREY GORDON: Inside of the hose?
MR. ASSAAD: Inside the hose.
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. Oh, inside the hose. You're not talking about the -- you know, the blower itself?
Q. The blow --
or the blower or anything.
A. Well Bernard, in his study, said he did it because he thought it was important.
Q. Okay. But have you looked at the operating room manual?
A. Have I looked --
Q. Yeah.
A. Oh, no. I haven't looked at that, no.

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Q. Why not?
A. I think I had enough to do I guess trying to get this report together, and...
Q. You spent over 300 hours, why not spend another hour on the report -- or looking at the manual?
MR. COREY GORDON: Object to the form of the question.
A. I mean -- I mean, I guess I'm more interested in the infections and the outcomes than, you know, how it worked, and so I didn't look at it.
Q. Do you know the difference between the Model 505 and the Model 750?
A. I understand there was a filter that was different.
Do I have the right -- Is that correct? I'm trying to think if I have the right statement.
Q. Well, I'm not going to answer questions. I'm asking you questions.
A. Yeah. No, that's --
Q. Do you know the difference in the airflow?
A. No.
Q. Do you know the difference in the amount of heat it produces?
A. No.

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Q. Do you know what a thermal plume is?
A. What is what?
Q. A thermal plume.
A. No. I would assume it's --
No, I don't know what it is, but.
(Discussion off the stenographic record.)
Q. Have you reviewed studies that indicate that when the Bair Hugger is turned on that it actually increases the temperature around the surgical table?
A. Yes, I think it does.
Q. So you agree with that?
A. At least some studies have, yeah.
Q. You don't dispute that; correct?
A. No.
Q. And it makes sense; right?
A. Makes sense, too.
Q. Yeah.
(Discussion off the stenographic record.)
Q. And you would agree that that -- that the Bair Hugger's blowing heat down underneath -- above the -- like over the patient and then it goes down towards underneath the operating room table; correct?
MR. COREY GORDON: Object to the form of the question, lack of foundation.
A. I think it goes down, but I'm -- I told you

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earlier I wasn't an expert in aerodynamics and --
Q. Okay.
A. -- didn't look at all those, you know, computational studies.
Q. You've written many research papers; correct?
A. Yes.
Q. Peer-reviewed papers; correct?
A. Yes.
Q. And do you agree with me that when you do a study, the paper should include enough methodology in the methods section so the study could be repeatable; correct?
A. Yes.
Q. Okay. And that's how you determine whether or not the study is reliable; correct?
A. Well it helps, yeah.
Q. Okay. Because with -- you know, repeatability is pretty much synonymous with reliability; correct?
A. Yeah, I would think that's reasonable.
Q. Now with respect to maintaining normothermia, you're not advocating for one device over another; are you?
A. In terms of general for the patients to

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remain?
Q. Yes.
A. No, I'm not. As long as the patients are warm, I think they'll probably do okay.
Q. So just so I understand, you're not here advocating that the Bair Hugger device is better than the Mistral device; correct?
A. Actually is that the one that's just been tested by Kurz; is that the Cleveland Clinic?
Q. Yes.
A. Yeah. Actually they look like they were the same, but there's actually, as you know, a lower rate with the Bair Hugger than with the HEPA filter forced-air warming, it's .44 versus .74 I think.
Q. Okay. Any criticism of that study?
A. It was a remarkably robust study. You're talking about 5,000 patients and they did something, you know, and they have the part of their prospective cohort, and they did multivariate analysis and they looked at comorbidities. So a huge study. And with the Bair Hugger a rate of .44, which I think is percent, that's as good as anywhere in the world.
Q. Well that's similar to what McGovern did, isn't it? He just -- They stopped using one product, then used another and they did a comparison; correct?

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A. Yeah. He left out all the issues related to confounding and bias, and --
Q. In the Cleveland Clinic study; correct?
A. No, no. The Cleveland Clinic has all the -- they have a multivariate analysis before they put out their report.
Q. Did they look at their infection rates overall during the time periods of 2013 and 2015?
A. Did they do what?
Q. Did they look at the infection rates overall, over all surgeries?
A. Umm --
Q. Do you know that, whether or not, whether they did that?
A. This is -- I think it was all prosthetic joint is what I recall, Kurz.
Q. You understand that Cleveland Clinic's a teaching hospital; correct?
A. It is.
Q. And they have a lot of residents; correct?
A. Correct.
Q. And infection rates may depend on the attending and the residents; correct?
A. There's some data for that, sure.
Q. There's a lot of data for that; correct?

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A. Yeah.
Q. And they didn't look at, you know, using the Mistral and the Bair Hugger at the same time, they looked at at different time periods; correct?
A. That's true.
Q. So there could be different physicians doing the surgeries; correct?
A. Yeah.
Q. Different residents?
A. Yeah.
Q. Okay. There could be different skin preps during those times in those two years?
A. Yeah, I don't know the answer to that.
Q. Exactly. We don't know the answer to that, do we? Okay.
A. I don't. Somebody might.
Q. We agree that --
Could you agree with me that the difference was not statistically significant?
A. Correct.
Q. Okay. You're not offering those criticisms for -- for that study; are you?
A. No. I would tell you right away exactly the data.
Q. But you're not offering, so I had to

actually pull them out of you; correct?
A. Well I gave --
MR. COREY GORDON: Object to the form of the question.
Q. Right?
A. I was trying -- I mean I was trying to get your answer to, you know, is there any difference between the two devices.
Q. And we haven't seen -- we haven't looked at the --
This is just the poster presentation; correct?
A. Yeah.
Q. Have you seen the manuscript?
A. I think I've seen the manuscript, I'm trying to remember, or at least a draft of something. It might be just an enlarged poster.
Q. Well which was it? Did you see --
I want to talk either about the manuscript or the poster. Which one you want to talk about?
A. Let's talk about the poster is fine.
Q. Have you looked at the manuscript?
A. I think I saw more data than just the poster, yeah.
Q. Okay. What data else did you see?

A. What?
Q. What other data did you see?
A. Besides what?
Q. I mean, what data did you see about that study with respect to the -- the Cleveland Clinic study besides the poster?
A. Well I'm not sure I saw anything, but I thought I saw an expanded poster, I guess. I don't -- I don't know.
Q. Is it in your box of documents?
A. I hope so.
MS. ZIMMERMAN: I didn't see it. I could be wrong.
THE WITNESS: Yeah, I'm sorry.
MS. ZIMMERMAN: No. No. That's all right.
Q. By the way, are there -- are there documents that you did not print up that you looked on -- that you have on your computer?
A. No.
Q. So every document you reviewed you printed up and highlighted or have done something with it.
A. Yeah. I don't like to read stuff on the computer.
Q. Okay.
A. I'm old.

MR. COREY GORDON: Gabe, I'll just represent, he hasn't -- the only thing he's seen is what was attached to Mont's report. There is no -- however you want to characterize it, there's no other data that he or I or anyone connected with the plaintiffs -- or with the -- with this litigation has seen.
Q. So you're sitting here advocating for the Bair Hugger as a better device than the Mistral?
A. I'm not advocating for them. I'm saying that after review of the literature I've come to the conclusion that the Bair Hugger is not linked in any way to harm.
Q. Okay. And what about -- I mean -- Strike that.
But with respect to patient warming, as long as the patient is kept warm, you don't care what method is used; correct?
A. Right now I think there are no data to show that if the patients are warmed by anything else, particularly after the Kurz study, you have that warmer as an additional one. It looked the same.
Q. Which warmer?
A. The HEPA -- the forced-air warmer. So that's probably the best data I could point to.

Q. Are you aware of the CDC indicating that there should be nothing in the OR that blows air?
MR. COREY GORDON: Object to the form of the question, mis --
A. I've read --
MR. COREY GORDON: -- misstates the -- mischaracterizes the evidence.
A. I've read the document where they said that, and actually looked at their in-progress, I guess, guideline from December 2016, and they really talk about the air-water interface when they're giving that statement.
I should also say that, because I wanted to be sure, I called the director of the CDC's quality healthcare, I forget what the -- that whole division that oversees HICPAC, and she told me they -- you know, this wasn't pertaining to forced-air warming, it was worry -- their big concern was when, you know, the heater-cooler unit was identified as a really source of serious infection.
Q. What was her name?
A. It is Denise A. Cardo.
Q. How do you spell that, for the court reporter?
A. C-A-R-D-O.

Q. And when did you contact her?
A. In the last couple weeks.
Q. Did you contact her at the request of counsel?
A. No. They didn't know I did that.
Q. Okay. Did you bill it on your -- in your invoice?
A. No, I didn't.
Q. Okay. And do you have a record of this conversation?
A. No, I don't.
Q. How did you get her phone number?
A. Called CDC, got ahold of her former assistant, because the numbers don't carry over sometime when there's some movement, and she said, well you need to talk to this person's assistant. Gave me the assistant, I left a message and asked her if there was a good time when I could call.
MR. ASSAAD: Take a break?
THE REPORTER: Please. Thank you.
(Recess taken from 4:57 to 5:05 p.m.)
BY MR. ASSAAD:
Q. Doctor, turning to page 62?
A. Okay.
Q. 62 begins your critique of the McGovern

study; correct?
A. The clinical arm.
Q. Yes. Of the McGovern study; correct?
A. Yeah. Yes.
Q. And you go on for about, from page 62 to page 68; correct?
A. Let me see. Yes.
Q. You did not do a critical critique of any other study that -- that you looked at, such as you did with the McGovern study; correct?
A. That's probably true.
Q. Okay. You didn't do any critiques of --
(Cell phone interruption.)
MR. COREY GORDON: Sorry.
Q. -- the Sessler study we just looked at; correct?
A. True.
Q. You didn't do any critical critiques of the Huang study; correct?
A. Yeah.
Q. Okay. Or the Moretti study; correct?
A. Yes.
Q. Okay. But you decided to have a meeting with Dr. Borak and Dr. Holford and yourself to discuss the McGovern study; correct?

MR. COREY GORDON: Object to the form of the question.
A. I mean, I was told -- asked to come to a meeting to meet them. That's really what there was, and we did discuss the study, yes, very much.
Q. How long did you --
It was the majority of your discussions; correct?
A. Probably, yeah.
Q. Okay. And you all got together and figured out a way to discredit the McGovern study; correct?
MR. COREY GORDON: Object to the form of the question.
A. I don't know if I would have used that term. To look at it critically.
Q. To look at the study critically; correct?
A. Yes. Yeah.
Q. And let me ask you this. Prior to agreeing to be an expert in this case did you look at the McGovern study?
A. No. I don't think I --
Q. Okay.
A. -- knew about it.
Q. Did you --
Did you do any research to determine whether

or not you agreed with the -- with the defense in this case before you agreed to be an expert?
A. I spent -- no, just a couple of days, you know. So I told you the -- one thing was the timing was good, it was interesting, it was a single case. And I thought, well, you know, it might be interesting to look at this, particularly if you're really just asked to learn and they pay you to learn, and that's how I thought about it.
Q. Well they didn't pay you to learn, they paid you to be an expert for them in this case.
MR. COREY GORDON: Object to the form of the question, lack of foundation, mischaracterizes the evidence.
Q. It's your understanding that 3M hired you just to learn?
A. 3M didn't hire me.
Q. The attorneys representing --
A. The attorneys did, yeah.
Q. And who do you think was paying the attorneys?
A. 3M.
Q. Okay. So it's your opinion that 3M or the attorneys hired you just to learn?
A. No. You just asked me why I sort of got

involved, because this is really why.
Q. Okay.
A. To get a task where you're actually reviewing the literature and getting paid for it --
Q. Well --
A. -- as well, so.
Q. -- you charged $300,000 or -- in this case; correct?
A. Yeah.
Q. Okay. And if you were not going to side with the defendant with respect to what their position is in the Bair Hugger, you would agree with me that they probably wouldn't pay you $300,000.
MR. COREY GORDON: Object to the form of the question, argumentative, lack of foundation.
A. You'll have to ask the -- you know, the legal team what they would have done if --
Q. At what point --
A. -- I mean at -- at some point, if I disagreed, it would be down there. I went -- As you know in my report, I've tried to put down what I learned, and again I'll give the phrase, read 'em and weep. That's what --
Q. At what point in time did you make the determination that the Bair Hugger doesn't increase

the risks of periprosthetic surgical -- periprosthetic joint infection?
A. You talking about generally, or in the first case, or what?
Q. In the life of Dr. Wenzel.
MR. COREY GORDON: Object to the form of the question.
A. I don't know exactly when, but towards the time of my report on -- on the first case I said I couldn't find any information that would really link that infection to the Bair Hugger. Got more complicated, as you know, very quickly, and I was surprised how -- how -- how the numbers grew.
Q. Assuming that the majority of periprosthetic joint infections are caused by airborne contamination, would that affect your opinions in this case?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical, assumes facts not in evidence.
A. It's hard for me to answer that because it's not only a hypothetical, it's something that I just can't find any data for. I don't agree with --
Q. I understand that.
But just assume, and I'm allowed to ask you hypotheticals to test your -- your methodology and

basis.
A. Umm-hmm.
Q. Assume that a hundred percent of periprosthetic joint infections are caused by airborne contamination in the operating room. Would that affect your opinion whether or not the Bair Hugger increases the risk of periprosthetic joint infections?
A. So the data are the --
MR. COREY GORDON: Same objections.
THE WITNESS: Yeah. I'm sorry.
A. The data are the same whatever the assumption is that I would base my opinion on.
Q. Well you were -- your assumption is that, I think it was 80 or 90 percent of periprosthetic joint infections are caused by the patient's flora.
A. That's correct.
Q. Okay. Assume that zero percent are caused by the patient's flora and a hundred percent are caused by contaminants in the air in the operating room. Would that affect your opinion based on the particle studies, Darouiche, Stocks, the neutral buoyant studies of whether or not the Bair Hugger increases the risk of periprosthetic joint infection?
MR. COREY GORDON: Same objections.
A. So for me the only clinical data you have is

McGovern, and I would go through the McGovern study as critically as I did regardless of what assumption.
Q. Well you agree with me that -- Strike that.
You're aware of the Legg studies; correct?
A. Yeah.
Q. The particle and the neutrally buoyant helium bubbles; correct?
A. Yeah, yeah.
Q. And that shows that when the Bair Hugger is turned on particles and helium bubbles increase over the surgical site; correct?
A. Yeah.
Q. Okay. And you're aware of the McGovern study also did a neutrally buoyant bubble test; correct?
A. Yes, I think that's right.
Q. Okay. And you're aware of the Sessler study, and if you looked at the raw data it would show an increase in particles.
MR. COREY GORDON: Object to the form of the question, mischaracterizes the evidence.
A. So bubbles and particles --
(Interruption by the reporter.)
Q. Okay. Bubbles and particles?
A. Bubbles and particles are surrogate markers

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for the real infection, and there were times when the Bair Hugger was on where the particles went up, the heat went up, the bubbles went up, yes.
Q. Okay. So assuming that airborne contamination is -- Strike that.
Assuming that with all these studies regarding increased particles, increased bubbles, okay, take into consideration Stocks' particle study and Darouiche's CFU study and periprosthetic joint infections, and assume that periprosthetic joint infections are caused by airborne contamination. Would that affect your opinions in this case of whether or not the Bair Hugger increases periprosthetic joint infections?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical, assumes facts not in evidence.
A. It's very hypothetical, and as I've told you, probably not because I would look at the McGovern study as the key clinical study that you're pointing to for the efficacy, or for the -- saying what you did about the Bair Hugger.
Q. So if the -- if -- if the Bair Hugger...
Let's make it even simpler.
A. Yeah.

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Q. Still the same assumption that periprosthetic infections are caused by airborne contamination.
A. Yeah.
Q. Okay. If the Bair Hugger increases the bacterial load over the surgical site, would that affect your opinion of whether or not the Bair Hugger increases periprosthetic joint infections?
A. Only if I could link the CFUs to infections in a straightforward way.
Q. Similar to what Darouiche did but a much bigger study.
A. Much bigger.
Q. Okay. So if you could link CFUs to infections and the Bair Hugger increased the CFUs over the surgical site, that would affect your opinions of whether or not the Bair Hugger increased the risk of periprosthetic joint infections.
A. Well in this hypothetical I'd want to know whether the -- whatever the assumptions were, including a hundred percent of infections from the air, does the Bair Hugger actually increase infections.
Q. Well assume --
A. That's the key question, not bubbles or

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particles.
Q. So are you dismissing Darouiche's article?
A. No.
Q. Okay.
A. I'd say that he said there is no causal relationship that he can identify here. You need a much bigger study.
Q. That's --
You think he said there was no causal relationship?
A. I thought he -- he said that this isn't definite cause-and-effect. If I'm wrong, let me see it.
Q. But just so I understand, my hypothetical is inaccurate because it's your opinion that 90 percent of these periprosthetic joint infections are caused by the patient's flora.
A. Could be.
MR. COREY GORDON: Object to the form of the question, mischaracterizes his testimony.
A. I mean I -- I think we disagree. You know, I think that if you ask me where the origin of the infections are, I think it's the microbiome in a high proportion of patients. It could be as high as 90.
Q. Okay. Could it be as low as 10 percent?

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A. No, I don't think so.
Q. Greater than 50 percent?
A. Absolutely.
Q. Greater than 70 percent?
A. Somewhere between 70 and 90.
Q. Okay. One of your criticisms on McGovern is that you look -- you state that they changed antibiotics during the study period; correct?
A. That's true.
Q. Okay. Did you look at the effect of the prophylactic antibiotics gentamicin plus teicoplanin as compared to just a -- I guess just the gentamicin that was used; correct?
A. Yes.
Q. Did you look at it's effect in other studies with respect to periprosthetic joint infections?
A. The comparison, you mean, --
Q. Yeah.
A. -- in other studies?
No, I don't think -- I didn't see any.
Q. If other studies existed that indicate that there was -- they were pretty much the same type of effect on periprosthetic joint infections, would you agree with me that you could remove them as a confounding factor in the study?

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MR. COREY GORDON: Object to the form of the question.
A. Well, I mean, first of all, no one would design a study where you're going to change three or four or five things. That's background. And the gentamicin, as you know, is primarily targeting gram-negatives and susceptible Staph, no MRSA, probably very little of the coagulation negative Staph. And in, I think it was Reed's testimony, he said it increased the return to hemodialysis units because of course those you're going to see more renal failure, increased pneumonias. And Reed at the end said, you know, we're not going to go with this any more. If you add the teicoplanin you're going to get coagulation negative Staph and you're going to get MRSA, as well Staph aureus, and, you know, in case you're at a hospital where they have VRE, vanc-resistant enterococcus, it's going to cover that.
I'm sorry. I'll take that away, it won't cover that. The last one.
Q. Well I'm not really word worried about renal failure here, we're talking about periprosthetic joint infection.
A. No, I understand --
Q. Okay.

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A. -- but there are a lot of reasons not to use that.
Q. Okay. Do you know what the difference in the reduction of periprosthetic infection rates between the two different types of antibiotics used in McGovern?
MR. COREY GORDON: Object to the form of the question.
A. I think the --
Well they were either the same or might have been a little higher in fact with the teicoplanin gent.
Q. But do you know whether or not there was a statistically significant difference --
A. Don't know.
Q. -- between -- with respect to periprosthetic joint infections?
A. No. I don't remember that.
Q. Okay. So it is possible, if there's no statistical significant difference between the incident of periprosthetic joint infections with different antibiotic regimes, it would not be a confounding factor.
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.

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A. You know, I'm always going to tell you things are possible.
Q. Well you're stating -- you're criticizing the study because they have switched the antibiotic -- prophylactic antibiotics during the study period; correct?
A. That's true.
MR. COREY GORDON: Object to the form of the question.
Q. Do you have any evidence that that change in the prophylactic antibiotics had an effect on the infection rates of the periprosthetic joint infections?
A. If you hold the antibiotics and the thromboprophylaxis the same, the rates are one percent and one percent. Two with the confounders.
Q. My question is: Do you have any evidence that the change in prophylactics have an effect on periprosthetic joint infections --
MR. COREY GORDON: Objection --
Q. -- in general?
MR. COREY GORDON: Objection, asked and answered.
A. That's the best I can offer you.
Q. So you're looking at the McGovern study for

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your opinion that the two different types of antibiotic regimes have an effect on periprosthetic joint infections.
MR. COREY GORDON: Object to the form of the question.
A. I don't know that I would say it that way.
I don't remember exactly when you look just at the antibiotic and all the other things are still moving, what the rates were.
Q. Well are you -- is there any article that you reviewed in your 300-some hours of literature review to indicate that there is a difference in infection rates between the two antibiotic regimes used in the McGovern study?
MR. COREY GORDON: Object to the form of the question.
A. No. I don't have any study I can point to for that.
Q. Okay. Were you aware of -- Strike that.
Figure 13 you're referring to --
A. What page are you on?
Q. Oh, page 67. You're relying on what Dr. Borak prepared; correct?
A. Yeah. He created the graph, so I used it.
Q. How many conversations did you have with Dr.

Borak and Dr. Holford?
A. Besides the meeting, not at all with Holford, and one conversation with Borak.
Q. In the past year and a half?
A. The whole time that we've known each other.
Q. Okay. Did you take notes during your meeting with Dr. Borak and Dr. Holford?
A. No. I don't think so -- Well I don't think so, no.
Q. Okay. On page 72?
A. Okay.
Q. The highlighted section says: "In the discovery phase of the trial, it has been shown that 7 studies showing safety of the Bair Hugger were not published, were kept secret."
A. Yeah.
Q. What makes you believe that they were kept secret?
A. Because they were never published. They were data that were not favorable to Augustine, and why didn't he publish them?
Q. That means he kept it secret?
A. That's what I think happened.
Q. So you think any study that people do that they decide not to publish is kept secret?

A. No, but if you have seven that makes me suspicious.
Q. Okay. So 3M has thousands of studies and tests done on the Bair Hugger that they never published, so are they keeping stuff secret?
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence.
A. I don't know how to answer that. I mean, what kind of studies are we talking about, were they comparis -- looking for harm?
Q. Computational fluid dynamic studies.
A. I don't know.
MR. COREY GORDON: Same objections, also lack of foundation.
Q. Schlieren studies.
You know what Schlieren is?
A. No.
Q. Calculations of whether or not the Bair Hugger disrupts laminar flow. Have you seen those?
A. No.
Q. Okay. So are they keeping all their studies secret?
MR. COREY GORDON: Object to the form of the question, assumes facts not in evidence, --
A. I don't know.

MR. COREY GORDON: -- lack of foundation.
Q. Have you ever met Dr. Scott Augustine?
A. Doctor who?
Q. Scott Augustine?
A. No, I haven't.
Q. Do you have an opinion of Dr. Scott Augustine?
MR. COREY GORDON: Object to the form of the question.
A. As -- In what way, opinion as to --
Q. As an inventor, as a doctor?
A. Well he's creative, obviously. The guy, you know, invented the Bair Hugger and I -- I would say he's a real entrepreneur. I have a lot of criticisms of his most recent study, if that's what you mean.
Q. That's not in your report, is it, sir?
A. No.
Q. Okay. Do you have any criticisms of the HotDog device?
A. Of the device itself?
Q. Yeah.
A. I'm not aware -- No, I...
No, I don't.
Q. And you've seen studies that show that the HotDog is just as efficacious as the Bair Hugger in

orthopedic surgeries.
A. I haven't seen that. But what it show -- if you're talking about particles or stuff like that?
Q. I'm talking about efficacy of warming patients.
A. No. There -- I don't think there are any data.
Q. Now is it my understanding that you would need a clinical study to -- Strike that.
If a device contaminates the sterile field, you would need a clinical study to show that it caused harm?
MR. COREY GORDON: Object to the form of the question, incomplete hypothetical.
A. I would say that would be a signal that would lead to a study that we would see whether or not that signal with, let's say, particles equate to infection, and that's what I would want to have.
Q. All right. You're a member of the International Society For Infectious Disease; correct?
A. That's true.
Q. Are you still a member?
A. Yeah. You're a kind of a member forever.
Q. Okay.
(Wenzel Exhibit 13 marked for

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identification.)
BY MR. ASSAAD:
Q. Do you recognize this document?
A. I do.
Q. It's titled, "A Guide to Infection Control in the Hospital, Fourth Edition"; correct?
A. Yes.
Q. And you're the editor; correct?
A. Yes.
Q. And we discussed this doc -- we discussed this book before; correct?
A. We did.
Q. Okay. And you had --
And you believe this is authoritative; correct?
A. Yeah, with the context I gave you what we're trying to do in poor countries where the resources are just limited, we tried to come up with some key points for healthcare workers.
Q. Are you saying this only applies to poor countries and not to the United States?
A. No, but that was the major -- that was the major thrust.
Q. But I would hope that you would treat, like, Third World countries the same as you would First

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World countries.
A. I would.
MR. COREY GORDON: Object to the form of the question.
Q. So I want to turn to Chapter 21. I only printed up Chapter 21.
A. Yes.
Q. Let's look at page -- paragraph on the bottom of page 134 that starts with "exogenous"?
A. Okay.
Q. And this is --
And you reviewed this before; correct?
A. I did see this.
Q. And you approved this for publication; correct?
A. I did.
Q. Okay. "Exogenous contamination of wounds is also important in the pathophysiology of SSIs, particularly for clean surgical procedures."
Did I read that correctly?
A. Yes.
Q. And a clean surgical -- a clean surgical procedure would be a total hip or total knee arthroplasty; correct?
A. That's correct.

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Q. "Airborne bacteria originating from the patient or the surgical team suffice to create SSI in these types of procedures, particularly when implants are being placed (example, total hip prostheses)."
Did I read that correctly?
A. You did.
Q. Okay. Those are the surgeries that are at issue in this case; correct?
A. Yes.
Q. Okay. Airborne contamination well well affect other clean surgical procedures with long exposure times and large surface areas, period.
Correct?
A. Yes.
Q. "The main source of airborne bacteria in the OR originate primarily from the skin of individuals in the room," period.
Did I read that correctly?
A. You did.
Q. "The number of persons present in the OR as well as their level of activity, the type of surgery, the quality of air provided, the rate of air exchange, the quality of staff clothing, the quality of cleaning process and the level of compliance with infection control practices all influence airborne

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contamination," period.
Did I read that correctly?
A. You did.
Q. And this is something that you agreed with at the time that it was published; correct?
A. Agreed that, yes.
Q. Okay. "Although these may seem trivial issues for contaminated procedures or dirty procedures, they are very important to consider in clean and clean-contaminated surgery," period.
Did I read that correctly?
A. You did.
Q. And that's something that you yourself as the -- the main editor, published in 2008; correct?
A. We did.
MR. ASSAAD: I have no more questions.
MR. COREY GORDON: I'll just have a couple.
EXAMINATION
BY MR. COREY GORDON:
Q. Keep Exhibit 13 open. That paragraph that counsel was just reading from in that sec -- Go back to page 134.
A. Sure.
Q. Under "Known Facts."
A. Yes.

Q. Could you just read the first sentence, please?
A. "Most SSIs arises from the patient's endogenous flora which contaminate the wound by direct contact."
Q. Thank you.
And if you could turn to page 138?
A. Yeah.
Q. And could you -- in the -- just read that first paragraph under "Controversial Issues" there.
A. "ORs equipped with laminar airflow system provide almost sterile air, yet a very few studies show a significant decrease in SSI rates for surgical procedures performed in this type of OR."
Q. And go ahead and read the rest of the paragraph.
A. "Furthermore, some of these experiments did not control for the antimicrobial regimen received as surgical prophylaxis, thus precluding any conclusion on the exact role of the laminar flow system. Therefore, at this time no recommendation can be made for the use of laminar flow ventilation in" the "ORs."
Q. This was published in 2008; is that right?
A. I think that's right. Yes.
Q. Thank you.

MR. COREY GORDON: I have nothing further.
MR. ASSAAD: I have one more question.
EXAMINATION
BY MR. ASSAAD:
Q. Go to page 134.
A. Oh, okay.
Q. When you read, "Most SSIs arise from the patient's endogenous flora which contaminate the wound by direct contact." "Direct contact" is -- is by -- by hand or some inanimate device; correct?
A. When I think of it I think that it's already there, as you know, we've talked about this before, and once the blade goes across that's direct contact with the wound. Now she may mean, in addition, you know, if there's a -- a scalpel that picks up part of the flora and then is used in the wound. I would have to go back and talk to her if -- what she meant more commonly, or both.
Q. But you understand bacteria -- when they talk about direct contact with bacteria, it's transferring it from, like, your hand to a device or your hand to a wound; correct?
A. That's correct.
MR. COREY GORDON: Object to the form of the question.

MR. ASSAAD: That's all I have.
THE WITNESS: Okay.
MR. COREY GORDON: We're done. We'll read and sign.
THE REPORTER: Off the record.
(Deposition concluded at 5:35 p.m.)

C E R T I F I C A T E

I, Debby J. Campeau, hereby certify that I am qualified as a verbatim shorthand reporter; that I took in stenographic shorthand the testimony of RICHARD P. WENZEL, M.D., MSc., at the time and place aforesaid; and that the foregoing transcript consisting of 368 pages is a true and correct, full and complete transcription of said shorthand notes, to the best of my ability.

Dated at Lino Lakes, Minnesota, this 9th day of August, 2017.

DEBBY J. CAMPEAU
Notary Public

S I G N A T U R E P A G E

I, RICHARD P. WENZEL, M.D., MSc., the deponent, hereby certify that I have read the foregoing transcript, consisting of 368 pages, and that said transcript is a true and correct, full and complete transcription of my deposition, except per the attached corrections, if any.

PAGE	LINE	CHANGE/REASON FOR CHANGE
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Date Signature of Witness

WITNESS MY HAND AND SEAL this _____ day of _____, 2017.

(DJC) _____

EXHIBIT DX3

TO DECLARATION OF MARY S. YOUNG IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE OPINIONS AND TESTIMONY OF RICHARD WENZEL, M.D.

UNITED STATES DISTRICT COURT
DISTRICT OF MINNESOTA

In Re:
Bair Hugger Forced Air Warming
Products Liability Litigation

This Document Relates To:

All Actions — MDL No. 15-2666 (JNE/FLM)

VIDEOTAPED DEPOSITION

OF

MARK ALBRECHT

VOLUME 1

Minneapolis, Minnesota

Friday, October 7th, 2016

Reported by:
Amy L. Larson, RPR
Job No. 112502

likely in the air.

Q. Okay. So did it surprise you that, you know, with -- with -- with operating rooms 1 and 3 having tens of thousands of particles being emitted, you couldn't culture out any bugs?

MR. B. GORDON: Objection to form, conflating particles and bugs again, but...

THE WITNESS: So to answer that, a large amount of the particles are going to be atmospheric dust that come in and so the -- it is not exactly surprising, because atmospheric dust is not bacteria always, it's not, it's just particles that are in the air.

BY MR. C. GORDON:

Q. And -- and to Mr. Ben Gordon's objection, particles don't correlate to bacteria, correct?

A. Correct.

MR. B. GORDON: Object to form.

BY MR. C. GORDON:

Q. And in, you know, kind of in lay terms, if we -- if somebody looks at a window on a very bright, sunny day and you see a bunch of stuff in the air, if you close the shades

STATE OF MINNESOTA)
) ss
COUNTY OF ANOKA)

Be it known that I took the foregoing deposition of Mark Albrecht, Volume 1, on October 7th, 2016, in Minneapolis, Minnesota;

That I was then and there a notary public in and for the County of Anoka, State of Minnesota, and that by virtue thereof, I was duly authorized to administer an oath;

That the witness was by me first duly sworn to testify to the truth, the whole truth and nothing but the truth relative to said cause;

That the foregoing transcript is a true and correct transcript of my stenographic notes in said matter;

That the witness reserved the right to read and sign the transcript;

That I am not related to any of the parties hereto, nor interested in the outcome of the action;

WITNESS MY HAND AND SEAL this 19th day of October, 2016.

_____

Amy L. Larson, RPR
My Commission Expires 1/31/2020

EXHIBIT DX4

TO DECLARATION OF MARY S. YOUNG IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE OPINIONS AND TESTIMONY OF RICHARD WENZEL, M.D.

SPECIAL ARTICLES

Guideline for Prevention of Surgical Site Infection, 1999

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U.S. Department of Health and Human Services

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Table of Contents

EXECUTIVE SUMMARY

The "Guideline for Prevention of Surgical Site Infection, 1999" presents the Centers for Disease Control and Prevention (CDC)'s recommendations for the prevention of surgical site infections (SSIs), formerly called surgical wound infections. This two-part guideline updates and replaces previous guidelines.[1,2]

Part I, "Surgical Site Infection: An Overview," describes the epidemiology, definitions, microbiology, pathogenesis, and surveillance of SSIs. Included is a detailed discussion of the pre-, intra-, and postoperative issues relevant to SSI genesis.

Part II, "Recommendations for Prevention of Surgical Site Infection," represents the consensus of the Hospital Infection Control Practices Advisory Committee (HICPAC) regarding strategies for the prevention of SSIs.[3] Whenever possible, the recommendations in Part II are based on data from well-designed scientific studies. However, there are a limited number of studies that clearly validate risk factors and prevention measures for SSI. By necessity, available studies have often been conducted in narrowly defined patient populations or for specific kinds of operations, making generalization of their findings to all specialties and types of operations potentially problematic. This is especially true regarding the implementation of SSI prevention measures. Finally, some of the infection control practices routinely used by surgical teams cannot be rigorously studied for ethical or logistical reasons (e.g., wearing vs not wearing gloves). Thus, some of the recommendations in Part II are based on a strong theoretical rationale and suggestive evidence in the absence of confirmatory scientific knowledge.

It has been estimated that approximately 75% of all operations in the United States will be performed in "ambulatory," "same-day," or "outpatient" operating rooms by the turn of the century.[4] In recommending various SSI prevention methods, this document makes no distinction between surgical care delivered in such settings and that provided in conventional inpatient operating rooms. This document is primarily intended for use by surgeons, operating room nurses, postoperative inpatient and clinic nurses, infection control professionals, anesthesiologists, healthcare epidemiologists, and other personnel directly responsible for the prevention of nosocomial infections.

This document does *not:*

- Specifically address issues unique to burns, trauma, transplant procedures, or transmission of bloodborne pathogens from healthcare worker to patient, nor does it specifically address details of SSI prevention in pediatric surgical practice. It has been recently shown in a multicenter study of pediatric surgical patients that characteristics related to the operations are more important than those related to the physiologic status of the patients.[5] In general, all SSI prevention measures effective in adult surgical care are indicated in pediatric surgical care.
- Specifically address procedures performed outside of the operating room (e.g., endoscopic proce-

dures), nor does it provide guidance for infection prevention for invasive procedures such as cardiac catheterization or interventional radiology. Nonetheless, it is likely that many SSI prevention strategies also could be applied or adapted to reduce infectious complications associated with these procedures.

- Specifically recommend SSI prevention methods unique to minimally invasive operations (i.e., laparoscopic surgery). Available SSI surveillance data indicate that laparoscopic operations generally have a lower or comparable SSI risk when contrasted to open operations.[6-11] SSI prevention measures applicable in open operations (e.g., open cholecystectomy) are indicated for their laparoscopic counterparts (e.g., laparoscopic cholecystectomy).
- Recommend specific antiseptic agents for patient preoperative skin preparations or for healthcare worker hand/forearm antisepsis. Hospitals should choose from products recommended for these activities in the latest Food and Drug Administration (FDA) monograph.[12]

I. Surgical Site Infection (SSI): An Overview

A. INTRODUCTION

Before the mid-19th century, surgical patients commonly developed postoperative "irritative fever," followed by purulent drainage from their incisions, overwhelming sepsis, and often death. It was not until the late 1860s, after Joseph Lister introduced the principles of antisepsis, that postoperative infectious morbidity decreased substantially. Lister's work radically changed surgery from an activity associated with infection and death to a discipline that could eliminate suffering and prolong life.

Currently, in the United States alone, an estimated 27 million surgical procedures are performed each year.[13] The CDC's National Nosocomial Infections Surveillance (NNIS) system, established in 1970, monitors reported trends in nosocomial infections in U.S. acute-care hospitals. Based on NNIS system reports, SSIs are the third most frequently reported nosocomial infection, accounting for 14% to 16% of all nosocomial infections among hospitalized patients.[14] During 1986 to 1996, hospitals conducting SSI surveillance in the NNIS system reported 15,523 SSIs following 593,344 operations (CDC, unpublished data). Among surgical patients, SSIs were the most common nosocomial infection, accounting for 38% of all such infections. Of these SSIs, two thirds were confined to the incision, and one third involved organs or spaces accessed during the operation. When surgical patients with nosocomial SSI died, 77% of the deaths were reported to be related to the infection, and the majority (93%) were serious infections involving organs or spaces accessed during the operation.

In 1980, Cruse estimated that an SSI increased a patient's hospital stay by approximately 10 days and cost an additional $2,000.[15,16] A 1992 analysis showed that each SSI resulted in 7.3 additional postoperative hospital days, adding $3,152 in extra charges.[17] Other studies corroborate that increased length of hospital stay and cost are associated with SSIs.[18,19] Deep SSIs involving organs or spaces, as compared to SSIs confined to the incision, are associated with even greater increases in hospital stays and costs.[20,21]

Advances in infection control practices include improved operating room ventilation, sterilization methods, barriers, surgical technique, and availability of antimicrobial prophylaxis. Despite these activities, SSIs remain a substantial cause of morbidity and mortality among hospitalized patients. This may be partially explained by the emergence of antimicrobial-resistant pathogens and the increased numbers of surgical patients who are elderly and/or have a wide variety of chronic, debilitating, or immunocompromising underlying diseases. There also are increased numbers of prosthetic implant and organ transplant operations performed. Thus, to reduce the risk of SSI, a systematic but realistic approach must be applied with the awareness that this risk is influenced by characteristics of the patient, operation, personnel, and hospital.

B. KEY TERMS USED IN THE GUIDELINE

1. Criteria for defining SSIs

The identification of SSI involves interpretation of clinical and laboratory findings, and it is crucial that a surveillance program use definitions that are consistent and standardized; otherwise, inaccurate or uninterpretable SSI rates will be computed and reported. The CDC's NNIS system has developed standardized surveillance criteria for defining SSIs (Table 1).[22] By these criteria, SSIs are classified as being either incisional or organ/space. Incisional SSIs are further divided into those involving only skin and subcutaneous tissue (superficial incisional SSI) and those involving deeper soft tissues of the incision (deep incisional SSI). Organ/space SSIs involve any part of the anatomy (e.g., organ or space) other than incised body wall layers, that

Table 1. Criteria for Defining a Surgical Site Infection (SSI)*

Superficial Incisional SSI

Infection occurs within 30 days after the operation *and* infection involves only skin or subcutaneous tissue of the incision *and* at least *one* of the following:

1. Purulent drainage, with or without laboratory confirmation, from the superficial incision.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue from the superficial incision.
3. At least one of the following signs or symptoms of infection: pain or tenderness, localized swelling, redness, or heat *and* superficial incision is deliberately opened by surgeon, *unless* incision is culture-negative.
4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.

Do *not* report the following conditions as SSI:

1. Stitch abscess (minimal inflammation and discharge confined to the points of suture penetration).
2. Infection of an episiotomy or newborn circumcision site.
3. Infected burn wound.
4. Incisional SSI that extends into the fascial and muscle layers (see deep incisional SSI).

Note: Specific criteria are used for identifying infected episiotomy and circumcision sites and burn wounds.[433]

Deep incisional SSI

Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* infection involves deep soft tissues (e.g., fascial and muscle layers) of the incision *and* at least *one* of the following:

1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
2. A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms: fever (>38°C), localized pain, or tenderness, unless site is culture-negative.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

Notes:

1. Report infection that involves both superficial and deep incision sites as deep incisional SSI.
2. Report an organ/space SSI that drains through the incision as a deep incisional SSI.

Organ/space SSI

Infection occurs within 30 days after the operation if no implant† is left in place or within 1 year if implant is in place and the infection appears to be related to the operation *and* infection involves any part of the anatomy (e.g., organs or spaces), other than the incision, which was opened or manipulated during an operation *and* at least *one* of the following:

1. Purulent drainage from a drain that is placed through a stab wound‡ into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

* Horan TC et al.[22]

†National Nosocomial Infection Surveillance definition: a nonhuman-derived implantable foreign body (e.g., prosthetic heart valve, nonhuman vascular graft, mechanical heart, or hip prosthesis) that is permanently placed in a patient during surgery.

‡If the area around a stab wound becomes infected, it is not an SSI. It is considered a skin or soft tissue infection, depending on its depth.

was opened or manipulated during an operation (Figure). Table 2 lists site-specific classifications used to differentiate organ/space SSIs. For example, in a patient who had an appendectomy and subsequently developed an intra-abdominal abscess not draining through the incision, the infection would be reported as an organ/space SSI at the intra-abdominal site. Failure to use objective criteria to define SSIs has been shown to substantially affect reported SSI rates.[23,24] The CDC NNIS definitions of SSIs have been applied consistently by surveillance and surgical personnel in many settings and currently are a de facto national standard.[22,25]

2. Operating suite

A physically separate area that comprises operating rooms and their interconnecting hallways and ancillary work areas such as scrub sink rooms. No distinction is made between operating suites located in conventional inpatient hospitals and those used for "same-day" surgical care, whether in a hospital or a free-standing facility.

3. Operating room

A room in an operating suite where operations are performed.

4. Surgical personnel

Any healthcare worker who provides care to surgical patients during the pre-, intra-, or postoperative periods.

5. Surgical team member

Any healthcare worker in an operating room during the operation who has a surgical care role. Members of the surgical team may be "scrubbed" or not; scrubbed members have direct contact with the sterile operating field or

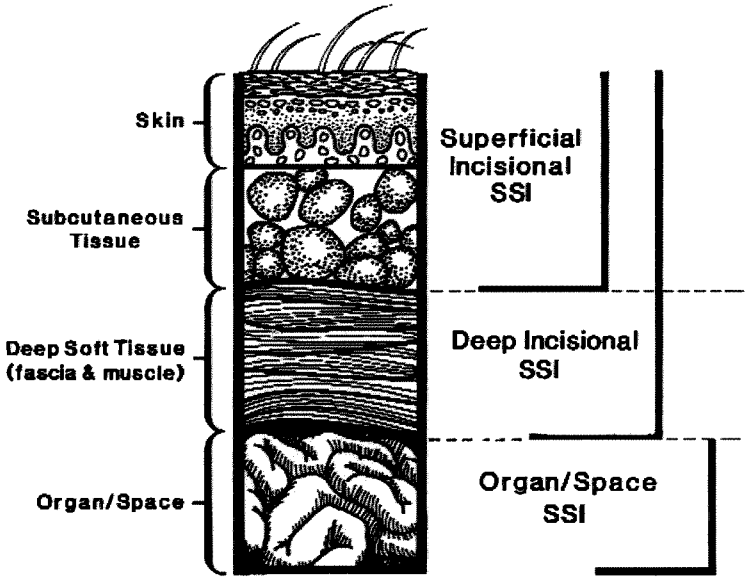

Figure. Cross-section of abdominal wall depicting CDC classifications of surgical site infection.[22]

sterile instruments or supplies used in the field (refer to "Preoperative Hand/Forearm Antisepsis" section).

C. MICROBIOLOGY

According to data from the NNIS system, the distribution of pathogens isolated from SSIs has not changed markedly during the last decade (Table 3).[26,27] *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterococcus* spp., and *Escherichia coli* remain the most frequently isolated pathogens. An increasing proportion of SSIs are caused by antimicrobial-resistant pathogens, such as methicillin-resistant *S. aureus* (MRSA),[28,29] or by *Candida albicans*.[30] From 1991 to 1995, the incidence of fungal SSIs among patients at NNIS hospitals increased from 0.1 to 0.3 per 1,000 discharges.[30] The increased proportion of SSIs caused by resistant pathogens and *Candida* spp. may reflect increasing numbers of severely ill and immunocompromised surgical patients and the impact of widespread use of broad-spectrum antimicrobial agents.

Outbreaks or clusters of SSIs have also been caused by unusual pathogens, such as *Rhizopus oryzae, Clostridium perfringens, Rhodococcus bronchialis, Nocardia farcinica, Legionella pneumophila* and *Legionella dumoffii,* and *Pseudomonas multivorans.* These rare outbreaks have been traced to contaminated adhesive dressings,[31] elastic bandages,[32] colonized surgical personnel,[33,34] tap water,[35] or contaminated disinfectant solutions.[36] When a cluster of SSIs involves an unusual organism, a formal epidemiologic investigation should be conducted.

D. PATHOGENESIS

Microbial contamination of the surgical site is a necessary precursor of SSI. The risk of SSI can be conceptualized according to the following relationship[37,38]:

$$\frac{\text{Dose of bacterial contamination} \times \text{virulence}}{\text{Resistance of the host patient}} = \text{Risk of surgical site infection}$$

Quantitatively, it has been shown that if a surgical site is contaminated with $>10^5$ microorganisms per gram of tissue, the risk of SSI is markedly increased.[39] However, the dose of contaminating microorganisms required to produce infection may be much lower when foreign material is present at the site (i.e., 100 staphylococci per gram of tissue introduced on silk sutures).[40-42]

Microorganisms may contain or produce toxins and other substances that increase their ability to invade a host, produce damage within the host, or survive on or in host tissue. For example, many gram-negative bacteria produce endotoxin, which stimulates cytokine production. In turn, cytokines can trigger the systemic inflammatory response syndrome that sometimes leads to multiple system organ failure.[43-45] One of the most common causes of multiple system organ failure in modern surgical care is intra-abdominal infection.[46,47] Some bacterial surface components, notably polysaccharide capsules, inhibit phagocytosis,[48] a critical and early host defense response to microbial contamination. Certain strains of clostridia and streptococci produce potent exotoxins that disrupt cell membranes or alter cellular metabolism.[49] A variety of microorgan-

Table 2. Site-Specific Classifications of Organ/Space Surgical Site Infection*

Arterial or venous infection	Meningitis or ventriculitis
Breast abscess or mastitis	Myocarditis or pericarditis
Disc space	Oral cavity (mouth, tongue, or gums)
Ear, mastoid	Osteomyelitis
Endocarditis	Other infections of the lower respiratory tract (e.g., abscess or empyema)
Endometritis	Other male or female reproductive tract
Eye, other than conjunctivitis	Sinusitis
Gastrointestinal tract	Spinal abscess without meningitis
Intra-abdominal, not specified elsewhere	Upper respiratory tract
Intracranial, brain abscess or dura	Vaginal cuff
Joint or bursa	
Mediastinitis	

*Horan TC et al.[22]

Table 3. Distribution of Pathogens Isolated* From Surgical Site Infections, National Nosocomial Infections Surveillance System, 1986 to 1996

	Percentage of isolates	
Pathogen	**1986-1989[179] (N=16,727)**	**1990-1996[26] (N=17,671)**
Staphylococcus aureus	17	20
Coagulase-negative staphylococci	12	14
Enterococcus spp.	13	12
Escherichia coli	10	8
Pseudomonas aeruginosa	8	8
Enterobacter spp.	8	7
Proteus mirabilis	4	3
Klebsiella pneumoniae	3	3
Other *Streptococcus* spp.	3	3
Candida albicans	2	3
Group D streptococci (non-enterococci)	—	2
Other gram-positive aerobes	—	2
Bacteroides fragilis	—	2

*Pathogens representing less than 2% of isolates are excluded.

isms, including gram-positive bacteria such as coagulase-negative staphylococci, produce glycocalyx and an associated component called "slime,"[50-55] which physically shields bacteria from phagocytes or inhibits the binding or penetration of antimicrobial agents.[56] Although these and other virulence factors are well defined, their mechanistic relationship to SSI development has not been fully determined.

For most SSIs, the source of pathogens is the endogenous flora of the patient's skin, mucous membranes, or hollow viscera.[57] When mucous membranes or skin is incised, the exposed tissues are at risk for contamination with endogenous flora.[58] These organisms are usually aerobic gram-positive cocci (e.g., staphylococci), but may include fecal flora (e.g., anaerobic bacteria and gram-negative aerobes) when incisions are made near the perineum or groin. When a gastrointestinal organ is opened during an operation and is the source of pathogens, gram-negative bacilli (e.g., *E. coli*), gram-positive organisms (e.g., enterococci), and sometimes anaerobes (e.g., *Bacillus fragilis*) are the typical SSI isolates. Table 4 lists operations and the likely SSI pathogens associated with them. Seeding of the operative site from a distant focus of infection can be another source of SSI pathogens,[59-68] particularly in patients who have a prosthesis or other implant placed during the operation. Such devices provide a nidus for attachment of the organism.[50,69-73]

Exogenous sources of SSI pathogens include surgical personnel (especially members of the surgical team),[74-78] the operating room environment (including air), and all tools, instruments, and materials brought to the sterile field during an operation (refer to "Intraoperative Issues" section). Exogenous flora are primarily aerobes, especially gram-positive organisms (e.g., staphylococci and streptococci). Fungi from endogenous and exogenous sources rarely cause SSIs, and their pathogenesis is not well understood.[79]

E. RISK AND PREVENTION

The term *risk factor* has a particular meaning in epidemiology and, in the context of SSI pathophysiol-

Table 4. Operations, Likely Surgical Site Infection (SSI) Pathogens, and References on Usage of Antimicrobial Prophylaxis*

Operations	Likely Pathogens†‡	References
Placement of all grafts, prostheses, or implants	*Staphylococcus aureus*; coagulase-negative staphylococci	269,282-284,290
Cardiac	*Staphylococcus aureus*; coagulase-negative staphylococci	251-253,462,463
Neurosurgery	*Staphylococcus aureus*; coagulase-negative staphylococci	241,249,258,259,261, 464,465
Breast	*Staphylococcus aureus;* coagulase-negative staphylococci	242,248
Ophthalmic Limited data: however, commonly used in procedures such as anterior segment resection, vitrectomy, and scleral buckles	*Staphylococcus aureus*; coagulase-negative staphylococci; streptococci; gram-negative bacilli	466
Orthopedic Total joint replacement Closed fractures/use of nails, bone plates, other internal fixation devices Functional repair without implant/device Trauma	*Staphylococcus aureus;* coagulase-negative staphylococci; gram-negative bacilli	60,243-246,254, 255,467-473
Noncardiac thoracic Thoracic (lobectomy, pneumonectomy, wedge resection, other noncardiac mediastinal procedures) Closed tube thoracostomy	*Staphylococcus aureus;* coagulase-negative staphylococci; *Streptococcus pneumoniae;* gram-negative bacilli	240,247,474,475
Vascular	*Staphylococcus aureus;* coagulase-negative staphylococci	250,463,476,477
Appendectomy	Gram-negative bacilli; anaerobes	263,452,478
Biliary tract	Gram-negative bacilli; anaerobes	260,262,479-484
Colorectal	Gram-negative bacilli; anaerobes	200,239,256,287 289,485-490
Gastroduodenal	Gram-negative bacilli; streptococci; oropharyngeal anaerobes (e.g., peptostreptococci)	256,257,491-493
Head and neck (major procedures with incision through oropharyngeal mucosa)	*Staphylococcus aureus*; streptococci; oropharyngeal anaerobes (e.g., peptostreptococci)	494-497
Obstetric and gynecologic	Gram-negative bacilli; enterococci; group B streptococci; anaerobes	270-280,435
Urologic May not be beneficial if urine is sterile	Gram-negative bacilli	267

*Refer to "Antimicrobial prophylaxis in surgery," The Medical Letter, 1997,[266] for current recommendations of antimicrobial agents and doses.
†Likely pathogens from both endogenous and exogenous sources.
‡Staphylococci will be associated with SSI following all types of operations.

ogy and prevention, strictly refers to a variable that has a significant, independent association with the development of SSI after a specific operation. Risk factors are identified by multivariate analyses in epidemiologic studies. Unfortunately, the term risk factor often is used in the surgical literature in a broad sense to include patient or operation features which, although associated with SSI development in univariate analysis, are not necessarily independent predictors.[80] The literature cited in the sections that follow includes risk factors identified by both univariate and multivariate analyses.

Table 5 lists patient and operation characteristics that may influence the risk of SSI development. These characteristics are useful in two ways: (1) they allow stratification of operations, making surveillance data more comprehensible; and, (2) knowledge of risk factors before certain operations may allow for targeted prevention measures. For example, if it is known that a patient has a remote site infection, the surgical team may reduce SSI risk by scheduling an operation after the infection has resolved.

An SSI prevention measure can be defined as an action or set of actions intentionally taken to reduce the risk of an SSI. Many such techniques are directed at reducing opportunities for microbial contamination of the patient's tissues or sterile surgical instruments; others are adjunctive, such as using antimicrobial prophylaxis or avoiding unnecessary traumatic tissue dissection. Optimum application of SSI prevention measures requires that a variety of patient and operation characteristics be carefully considered.

1. Patient characteristics

In certain kinds of operations, patient characteristics possibly associated with an increased risk of an SSI include coincident remote site infections [59-68] or colonization,[81-83] diabetes,[84-87] cigarette smoking,[85,88-92] systemic steroid use,[84,87,93] obesity (>20% ideal body weight),[85-87,94-97] extremes of age,[92,98-102] poor nutritional status,[85,94,98,103-105] and perioperative transfusion of certain blood products.[106-109]

a. Diabetes

The contribution of diabetes to SSI risk is controversial,[84-86,98,110] because the independent contribution of diabetes to SSI risk has not typically been assessed after controlling for potential confounding factors. Recent preliminary findings from a study of patients who underwent coronary artery bypass graft showed a significant relationship between increasing levels of HgA1c and SSI rates.[111] Also, increased glucose levels (>200 mg/dL) in the immediate postoperative period (≤48 hours) were associated with increased SSI risk.[112,113] More studies are needed to assess the efficacy of perioperative blood glucose control as a prevention measure.

b. Nicotine use

Nicotine use delays primary wound healing and may increase the risk of SSI.[85] In a large prospective study, current cigarette smoking was an independent risk factor for sternal and/or mediastinal SSI following cardiac surgery.[85] Other studies have corroborated cigarette smoking as an important SSI risk factor.[88-92] The limitation of these studies, however, is that terms like *current cigarette smoking* and *active smokers* are not always defined. To appropriately determine the contribution of tobacco use to SSI risk, standardized definitions of smoking history must be adopted and used in studies designed to control for confounding variables.

c. Steroid use

Patients who are receiving steroids or other immunosuppressive drugs preoperatively may be predisposed to developing SSI,[84,87] but the data supporting this relationship are contradictory. In a study of long-term steroid use in patients with Crohn's disease, SSI developed significantly more often in patients receiving preoperative steroids (12.5%) than in patients without steroid use (6.7%).[93] In contrast, other investigations have not found a relationship between steroid use and SSI risk.[98,114,115]

d. Malnutrition

For some types of operations, severe protein-calorie malnutrition is crudely associated with postoperative nosocomial infections, impaired wound healing dynamics, or death.[116-124] The National Academy of Sciences/National Research Council (NAS/NRC),[94] Study on the Efficacy of Infection Control (SENIC),[125] and NNIS[126] schemes for SSI risk stratification do not explicitly incorporate nutritional status as a predictor variable, although it may be represented indirectly in the latter two. In a widely quoted 1987 study of 404 high-risk general surgery operations, Christou and coworkers derived an SSI probability index in which final predictor variables were patient age, operation duration, serum albumin level, delayed hypersensitivity test score, and intrinsic wound contamination level.[117] Although this index predicted SSI risk satisfactorily for 404 subsequent patients and was generally received as a significant advance in SSI risk stratification, it is not widely used in SSI surveillance data analysis, surgical infection research, or analytic epidemiology.

Theoretical arguments can be made for a belief that severe preoperative malnutrition should increase the risk of both incisional and organ/space SSI. However, an epidemiologic association between incisional SSI and malnutrition is difficult to demonstrate consistently for all surgical subspecialties.[118-120,124,127-131] Multivariate logistic regression modeling has shown that preoperative protein-calorie malnutrition is not an independent predictor of mediastinitis after cardiac bypass operations.[85,132]

In the modern era, total parenteral nutrition (TPN) and total enteral alimentation (TEA) have enthusiastic acceptance by surgeons and critical care specialists.[118,133-137] However, the benefits of preoperative nutritional repletion of malnourished patients in reducing

Table 5. Patient and Operation Characteristics That May Influence the Risk of Surgical Site Infection Development

Patient
Age
Nutritional status
Diabetes
Smoking
Obesity
Coexistent infections at a remote body site
Colonization with microorganisms
Altered immune response
Length of preoperative stay
Operation
Duration of surgical scrub
Skin antisepsis
Preoperative shaving
Preoperative skin prep
Duration of operation
Antimicrobial prophylaxis
Operating room ventilation
Inadequate sterilization of instruments
Foreign material in the surgical site
Surgical drains
Surgical technique
Poor hemostasis
Failure to obliterate dead space
Tissue trauma

Adapted from references 25, 37.

SSI risk are unproven. In two randomized clinical trials, preoperative "nutritional therapy" did not reduce incisional and organ/space SSI risk.[138-141] In a recent study of high-risk pancreatectomy patients with cancer, the provision of TPN preoperatively had no beneficial effect on SSI risk.[142] A randomized prospective trial involving 395 general and thoracic surgery patients compared outcomes for malnourished patients preoperatively receiving either a 7- to 15-day TPN regimen or a regular preoperative hospital diet. All patients were followed for 90 days postoperatively. There was no detectable benefit of TPN administration on the incidence of incisional or organ/space SSI.[143] Administering TPN or TEA may be indicated in a number of circumstances, but such repletion cannot be viewed narrowly as a prevention measure for organ/space or incisional SSI risk. When a major elective operation is necessary in a severely malnourished patient, experienced surgeons often use both pre- and postoperative nutritional support in consideration of the major morbidity associated with numerous potential complications, only one of which is organ/space SSI.[118,124,130,133,137,138,144-149] In addition, postoperative nutritional support is important for certain major oncologic operations,[135,136] after many operations on major trauma victims,[134] or in patients suffering a variety of catastrophic surgical complications that preclude eating or that trigger a hypermetabolic state. Randomized clinical trials will be necessary to determine if nutritional support alters SSI risk in specific patient-operation combinations.

e. Prolonged preoperative hospital stay

Prolonged preoperative hospital stay is frequently suggested as a patient characteristic associated with increased SSI risk. However, length of preoperative stay is likely a surrogate for severity of illness and co-morbid conditions requiring inpatient work-up and/or therapy before the operation.[16,26,65,85,94,100,150,151]

f. Preoperative nares colonization with *Staphylococcus aureus*

S. aureus is a frequent SSI isolate. This pathogen is carried in the nares of 20% to 30% of healthy humans.[81] It has been known for years that the development of SSI involving *S. aureus* is definitely associated with preoperative nares carriage of the organism in surgical patients.[81] A recent multivariate analysis demonstrated that such carriage was the most powerful independent risk factor for SSI following cardiothoracic operations.[82]

Mupirocin ointment is effective as a topical agent for eradicating *S. aureus* from the nares of colonized patients or healthcare workers. A recent report by Kluytmans and coworkers suggested that SSI risk was reduced in patients who had cardiothoracic operations when mupirocin was applied preoperatively to their nares, regardless of carrier status.[152] In this study, SSI rates for 752 mupirocin-treated patients were compared with those previously observed for an untreated group of 928 historical control patients, and the significant SSI rate reduction was attributed to the mupirocin treatment. Concerns have been raised regarding the comparability of the two patient groups.[153] Additionally, there is concern that mupirocin resistance may emerge, although this seems unlikely when treatment courses are brief.[81] A prospective, randomized clinical trial will be necessary to establish definitively that eradication of nasal carriage of *S. aureus* is an effective SSI prevention method in cardiac surgery. Such a trial has recently been completed on 3,909 patients in Iowa.[83] Five types of operations in two facilities were observed. Preliminary analysis showed a significant association between nasal carriage of *S. aureus* and subsequent SSI development. The effect of mupirocin on reducing SSI risk is yet to be determined.

g. Perioperative transfusion

It has been reported that perioperative transfusion of leukocyte-containing allogeneic blood components is an apparent risk factor for the development of postoperative bacterial infections, including SSI.[106] In three of five randomized trials conducted in patients undergoing elective colon resection for cancer, the risk of SSI was at least doubled in patients receiving blood transfusions.[107-109] However, on the basis of detailed epidemiologic reconsiderations, as many as 12 confounding variables may have influenced the reported association, and any effect of transfusion on SSI risk may be either small or nonexistent.[106] Because of methodologic problems, including the timing of transfusion, and use of nonstandardized SSI definitions, interpretation of the available data is limited. A meta-analysis of published trials will probably be required for resolution of the controversy.[154] There is currently no scientific basis for withholding necessary blood products from surgical patients as a means of either incisional or organ/space SSI risk reduction.

2. Operative characteristics: Preoperative issues

a. Preoperative antiseptic showering

A preoperative antiseptic shower or bath decreases skin microbial colony counts. In a study of >700 patients who received two preoperative antiseptic showers, chlorhexidine reduced bacterial colony counts ninefold (2.8×10^2 to 0.3), while povidone-iodine or triclocarban-medicated soap reduced colony counts by 1.3- and 1.9-fold, respectively.[155] Other studies corroborate these findings.[156,157] Chlorhexidine gluconate-containing products require several applications to attain maximum antimicrobial benefit, so repeated antiseptic showers are usually indicated.[158] Even though preoperative showers reduce the skin's microbial colony counts, they have not definitively been shown to reduce SSI rates.[159-165]

Table 6. Mechanism and Spectrum of Activity of Antiseptic Agents Commonly Used for Preoperative Skin Preparation and Surgical Scrubs

Agent	Mechanism of Action	Gram-Positive Bacteria	Gram-Negative Bacteria	Mtb	Fungi	Virus	Rapidity of Action	Residual Activity	Toxicity	Uses
Alcohol	Denature proteins	E	E	G	G	G	Most rapid	None	Drying, volatile	SP, SS
Chlorhexidine	Disrupt cell membrane	E	G	P	F	G	Intermediate	E	Ototoxicity, keratitis	SP, SS
Iodine/ Iodophors	Oxidation/ substitution by free iodine	E	G	G	G	G	Intermediate	Minimal	Absorption from skin with possible toxicity, skin irritation	SP, SS
PCMX	Disrupt cell wall	G	F*	F	F	F	Intermediate	Good	More data needed	SS
Triclosan	Disrupt cell wall	G	G	G	P	U	Intermediate	E	More data needed	SS

Abbreviations: E, excellent; F, fair; G, good; Mtb, Mycobacterium tuberculosis; P, poor; PCMX, para-chloro-meta-xylenol; SP, skin preparation; SS, surgical scrubs; U, unknown.
Data from Larson E.[176]
*Fair, except for *Pseudomonas* spp.; activity improved by addition of chelating agent such as EDTA.

b. Preoperative hair removal

Preoperative shaving of the surgical site the night before an operation is associated with a significantly higher SSI risk than either the use of depilatory agents or no hair removal.[16,100,166-169] In one study, SSI rates were 5.6% in patients who had hair removed by razor shave compared to a 0.6% rate among those who had hair removed by depilatory or who had no hair removed.[166] The increased SSI risk associated with shaving has been attributed to microscopic cuts in the skin that later serve as foci for bacterial multiplication. Shaving immediately before the operation compared to shaving within 24 hours preoperatively was associated with decreased SSI rates (3.1% vs 7.1%); if shaving was performed >24 hours prior to operation, the SSI rate exceeded 20%.[166] Clipping hair immediately before an operation also has been associated with a lower risk of SSI than shaving or clipping the night before an operation (SSI rates immediately before = 1.8% vs night before = 4.0%).[170-173] Although the use of depilatories has been associated with a lower SSI risk than shaving or clipping,[166,167] depilatories sometimes produce hypersensitivity reactions.[166] Other studies showed that preoperative hair removal by any means was associated with increased SSI rates and suggested that no hair be removed.[100,174,175]

c. Patient skin preparation in the operating room

Several antiseptic agents are available for preoperative preparation of skin at the incision site (Table 6). The iodophors (e.g., povidone-iodine), alcohol-containing products, and chlorhexidine gluconate are the most commonly used agents. No studies have adequately assessed the comparative effects of these preoperative skin antiseptics on SSI risk in well-controlled, operation-specific studies.

Alcohol is defined by the FDA as having one of the following active ingredients: ethyl alcohol, 60% to 95% by volume in an aqueous solution, or isopropyl alcohol, 50% to 91.3% by volume in an aqueous solution.[12] Alcohol is readily available, inexpensive, and remains the most effective and rapid-acting skin antiseptic.[176] Aqueous 70% to 92% alcohol solutions have germicidal activity against bacteria, fungi, and viruses, but spores can be resistant.[176,177] One potential disadvantage of the use of alcohol in the operating room is its flammability.[176-178]

Both chlorhexidine gluconate and iodophors have broad spectra of antimicrobial activity.[177,179-181] In some comparisons of the two antiseptics when used as preoperative hand scrubs, chlorhexidine gluconate achieved greater reductions in skin microflora than did povidone-iodine and also had greater residual activity after a single application.[182-184] Further, chlorhexidine gluconate is not inactivated by blood or serum proteins.[176,179,185,186] Iodophors may be inactivated by blood or serum proteins, but exert a bacteriostatic effect as long as they are present on the skin.[178,179]

Before the skin preparation of a patient is initiated, the skin should be free of gross contamination (i.e., dirt, soil, or any other debris).[187] The patient's skin is prepared by applying an antiseptic in concentric circles, beginning in the area of the proposed incision. The prepared area should be large enough to extend the incision or create new incisions or drain sites, if necessary.[1,177,187] The application of the skin preparation may need to be modified, depending on the condition of the skin (e.g., burns) or location of the incision site (e.g., face).

There are reports of modifications to the procedure for preoperative skin preparation which include: (1) removing or wiping off the skin preparation antiseptic agent after application, (2) using an antiseptic-impregnated adhesive drape, (3) merely painting the skin with an antiseptic in lieu of the skin preparation procedure described above, or (4) using a "clean" versus a "sterile" surgical skin preparation kit.[188-191] However, none of these modifications has been shown to represent an advantage.

d. Preoperative hand/forearm antisepsis

Members of the surgical team who have direct contact with the sterile operating field or sterile instruments or supplies used in the field wash their hands and forearms by performing a traditional procedure known as scrubbing (or the surgical scrub) immediately before donning sterile gowns and gloves. Ideally, the optimum antiseptic used for the scrub should have a broad spectrum of activity, be fast-acting, and have a persistent effect.[1,192,193] Antiseptic agents commercially available in the United States for this purpose contain alcohol, chlorhexidine, iodine/iodophors, para-chloro-meta-xylenol, or triclosan (Table 6).[176,177,179,194,195] Alcohol is considered the gold standard for surgical hand preparation in several European countries.[196-199] Alcohol-containing products are used less frequently in the United States than in Europe, possibly because of concerns about flammability and skin irritation. Povidone-iodine and chlorhexidine gluconate are the current agents of choice for most U.S. surgical team members.[177] However, when 7.5% povidone-iodine or 4% chlorhexidine gluconate was compared to alcoholic chlorhexidine (60% isopropanol and 0.5% chlorhexidine gluconate in 70% isopropanol), alcoholic chlorhexidine was found to have greater residual antimicrobial activity.[200,201] No agent is ideal for every situation, and a major factor, aside from the efficacy of any product, is its acceptability by operating room personnel after repeated use. Unfortunately, most studies evaluating surgical scrub antiseptics have focused on measuring hand bacterial colony counts. No clinical trials have evaluated the impact of scrub agent choice on SSI risk.[195,202-206]

Factors other than the choice of antiseptic agent influence the effectiveness of the surgical scrub. Scrubbing technique, the duration of the scrub, the condition of the hands, or the techniques used for drying and gloving are examples of such factors. Recent studies suggest that scrubbing for at least 2 minutes is as effective as the traditional 10-minute scrub in reducing hand bacterial colony counts,[207-211] but the optimum duration of scrubbing is not known. The first scrub of the day should include a thorough cleaning underneath fingernails (usually with a brush).[180,194,212] It is not clear that such cleaning is a necessary part of subsequent scrubs during the day. After performing the surgical scrub, hands should be kept up and away from the body (elbows in flexed position) so that water runs from the tips of the fingers toward the elbows. Sterile towels should be used for drying the hands and forearms before the donning of a sterile gown and gloves.[212]

A surgical team member who wears artificial nails may have increased bacterial and fungal colonization of the hands despite performing an adequate hand scrub.[212,213] Hand carriage of gram-negative organisms has been shown to be greater among wearers of artificial nails than among non-wearers.[213] An outbreak of *Serratia marcescens* SSIs in cardiovascular surgery patients was found to be associated with a surgical nurse who wore artificial nails.[214] While the relationship between nail length and SSI risk is unknown, long nails—artificial or natural—may be associated with tears in surgical gloves.[177,180,212] The relationship between the wearing of nail polish or jewelry by surgical team members and SSI risk has not been adequately studied.[194,212,215-217]

e. Management of infected or colonized surgical personnel

Surgical personnel who have active infections or are colonized with certain microorganisms have been linked to outbreaks or clusters of SSIs.[33,34,76,218-237] Thus, it is important that healthcare organizations implement policies to prevent transmission of microorganisms from personnel to patients. These policies should address management of job-related illnesses, provision of postexposure prophylaxis after job-related exposures and, when necessary, exclusion of ill personnel from work or patient contact. While work exclusion policies should be enforceable and include a statement of authority to exclude ill personnel, they should also be designed to encourage personnel to report their illnesses and exposures and not penalize personnel with loss of wages, benefits, or job status.[238]

f. Antimicrobial prophylaxis

Surgical antimicrobial prophylaxis (AMP) refers to a very brief course of an antimicrobial agent initiated just before an operation begins.[239-265] AMP is not an attempt to sterilize tissues, but a critically timed adjunct used to reduce the microbial burden of intraoperative contamination to a level that cannot overwhelm host defenses. AMP does not pertain to prevention of SSI caused by postoperative contamination.[265] Intravenous infusion is the mode of AMP delivery used most often in modern surgical practice.[20,26,242,266-281] Essentially all confirmed AMP indications pertain to elective operations in which skin incisions are closed in the operating room.

Four principles must be followed to maximize the benefits of AMP:

- Use an AMP agent for all operations or classes of operations in which its use has been shown to reduce SSI rates based on evidence from clinical trials or for those operations after which incisional or organ/space SSI would represent a catastrophe.[266,268,269,282-284]
- Use an AMP agent that is safe, inexpensive, and bactericidal with an in vitro spectrum that covers the most probable intraoperative contaminants for the operation.
- Time the infusion of the initial dose of antimicrobial agent so that a bactericidal concentration of the drug is established in serum and tissues by the time the skin is incised.[285]
- Maintain therapeutic levels of the antimicrobial agent in both serum and tissues throughout the operation and until, at most, a few hours after the incision is closed in the operating room.[179,266-268,282,284,286] Because clotted blood is present in all surgical wounds, therapeutic serum levels of AMP agents are logically important in addition to therapeutic tissue levels. Fibrin-enmeshed bacteria may be resistant to phagocytosis or to contact with antimicrobial agents that diffuse from the wound space.

Table 4 summarizes typical SSI pathogens according to operation type and cites studies that establish AMP efficacy for these operations. A simple way to organize AMP indications is based on using the surgical wound classification scheme shown in Table 7, which employs descriptive case features to *postoperatively* grade the degree of intraoperative microbial contamination. A surgeon makes the decision to use AMP by anticipating *preoperatively* the surgical wound class for a given operation.

AMP is indicated for all operations that entail entry into a hollow viscus under controlled conditions. The most frequent SSI pathogens for such clean-contaminated operations are listed in Table 4. Certain clean-contaminated operations, such as elective colon resection, low anterior resection of the rectum, and abdominoperineal resection of the rectum, also require an additional preoperative protective maneuver called "preparation of the colon," to empty the bowel of its contents and to reduce the levels of live microorganisms.[200,239,256,268,284,287] This maneuver includes the administration of enemas and cathartic agents followed by the oral administration of nonabsorbable antimicrobial agents in divided doses the day before the operation.[200,288,289]

AMP is sometimes indicated for operations that entail incisions through normal tissue and in which no viscus is entered and no inflammation or infection is encountered. Two well-recognized AMP indications for such clean operations are: (1) when any intravascular prosthetic material or a prosthetic joint will be inserted, and (2) for any operation in which an incisional or organ/space SSI would pose catastrophic risk. Examples are all cardiac operations, including cardiac pacemaker placement, [290] vascular operations involving prosthetic arterial graft placement at any site or the revascularization of the lower extremity, and most neurosurgical operations (Table 4). Some have advocated use of AMP during all operations on the breast.[80,242,264]

By definition, AMP is not indicated for an operation classified in Table 7 as contaminated or dirty. In such operations, patients are frequently receiving therapeutic antimicrobial agents perioperatively for established infections.

Cephalosporins are the most thoroughly studied AMP agents.[284] These drugs are effective against many gram-positive and gram-negative microorganisms. They also share the features of demonstrated safety, acceptable pharmacokinetics, and a reasonable cost per dose.[242] In particular, cefazolin is widely used and generally viewed as the AMP agent of first choice for clean operations.[266] If a patient is unable to receive a cephalosporin because of penicillin allergy, an alternative for gram-positive bacterial coverage is either clindamycin or vancomycin.

Cefazolin provides adequate coverage for many clean-contaminated operations, [268,291] but AMP for operations on the distal intestinal tract mandates use of an agent such as cefoxitin (or some other second-genera-

Table 7. Surgical Wound Classification

Class I/Clean: An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tract is not entered. In addition, clean wounds are primarily closed and, if necessary, drained with closed drainage. Operative incisional wounds that follow nonpenetrating (blunt) trauma should be included in this category if they meet the criteria.

Class II/Clean-Contaminated: An operative wound in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions and without unusual contamination. Specifically, operations involving the biliary tract, appendix, vagina, and oropharynx are included in this category, provided no evidence of infection or major break in technique is encountered.

Class III/Contaminated: Open, fresh, accidental wounds. In addition, operations with major breaks in sterile technique (e.g., open cardiac massage) or gross spillage from the gastrointestinal tract, and incisions in which acute, nonpurulent inflammation is encountered are included in this category.

Class IV/Dirty-Infected: Old traumatic wounds with retained devitalized tissue and those that involve existing clinical infection or perforated viscera. This definition suggests that the organisms causing postoperative infection were present in the operative field before the operation.

Garner JS[1] and Simmons BP.[2]

tion cephalosporin) that provides anaerobic coverage. If a patient cannot safely receive a cephalosporin because of allergy, a reasonable alternative for gram-negative coverage is aztreonam. However, an agent such as clindamycin or metronidazole should also be included to ensure anaerobic coverage.

The aminoglycosides are seldom recommended as first choices for AMP, either as single drugs or as components of combination regimens.[242,264] References cited in Table 4 provide many details regarding AMP choices and dosages, antimicrobial spectra and properties, and other practical clinical information.

The routine use of vancomycin in AMP is not recommended for any kind of operation.[242,266,283,292] However, vancomycin may be the AMP agent of choice in certain clinical circumstances, such as when a cluster of MRSA mediastinitis or incisional SSI due to methicillin-resistant coagulase-negative staphylococci has been detected. A threshold has not been scientifically defined that can support the decision to use vancomycin in AMP. The decision should involve consideration of local frequencies of MRSA isolates, SSI rates for particular operations, review of infection prevention practices for compliance, and consultation between surgeons and infectious disease experts. An effective SSI surveillance program must be operational, with careful and timely culturing of SSI isolates to determine species and AMP agent susceptibilities.[80]

Agents most commonly used for AMP (i.e., cephalosporins) exhibit time-dependent bactericidal action. The therapeutic effects of such agents are probably maximized when their levels continuously exceed a threshold value best approximated by the minimal bactericidal concentration value observed for the target pathogens in vitro. When the duration of an operation is expected to exceed the time in which therapeutic levels of the AMP agent can be maintained, additional AMP agent should be infused. That time point for cefazolin is estimated as 3 to 4 hours. In general, the timing of a second (or third, etc.) dose of any AMP drug is estimated from three parameters: tissue levels achieved in normal patients by a standard therapeutic dose, the approximate serum half-life of the drug, and awareness of approximate MIC_{90} values for anticipated SSI pathogens. References in Table 6 should be consulted for these details and important properties of antimicrobial agents used for AMP in various specialties.

Basic "rules of thumb" guide decisions about AMP dose sizes and timing. For example, it is believed that a full therapeutic dose of cefazolin (1-2 g) should be given to adult patients no more than 30 minutes before the skin is incised.[242,285] There are a few exceptions to this basic guide. With respect to dosing, it has been demonstrated that larger doses of AMP agents are necessary to achieve optimum effect in morbidly obese patients.[293] With respect to timing, an exception occurs for patients undergoing cesarean section in whom AMP is indicated: the initial dose is administered immediately after the umbilical cord is clamped.[266,272,273] If vancomycin is used, an infusion period of approximately 1 hour is required for a typical dose. Clearly, the concept of "on-call" infusion of AMP is flawed simply because delays in transport or schedule changes can mean that suboptimal tissue and serum levels may be present when the operation starts.[242,294] Simple protocols of AMP timing and oversight responsibility should be locally designed to be practical and effective.

3. Operative characteristics: Intraoperative issues

a. Operating room environment

(1) Ventilation

Operating room air may contain microbial-laden dust, lint, skin squames, or respiratory droplets. The microbial level in operating room air is directly proportional to the number of people moving about in the room.[295] Therefore, efforts should be made to minimize personnel traffic during operations. Outbreaks of SSIs caused by group A beta-hemolytic streptococci have been traced to airborne transmission of the organism from colonized operating room personnel to patients.[233,237,296,297] In these outbreaks, the strain causing the outbreak was recovered from the air in the operating room.[237,296] It has been demonstrated that exercising and changing of clothing can lead to airborne dissemination of group A streptococci from vaginal or rectal carriage.[233,234,237,297]

Operating rooms should be maintained at positive pressure with respect to corridors and adjacent areas.[298] Positive pressure prevents airflow from less clean areas into more clean areas. All ventilation or air conditioning systems in hospitals, including those in operating rooms, should have two filter beds in series, with the efficiency of the first filter bed being ≥30% and that of the second filter bed being ≥90%.[299] Conventional operating room ventilation systems produce a minimum of about 15 air changes of filtered air per hour, three (20%) of which must be fresh air.[299,300] Air should be introduced at the ceiling and exhausted near the floor.[300,301] Detailed ventilation parameters for operating rooms have been published by the American Institute of Architects in collaboration with the U.S. Department of Health and Human Services (Table 8).[299]

Laminar airflow and use of UV radiation have been suggested as additional measures to reduce SSI risk for certain operations. Laminar airflow is designed to move particle-free air (called "ultraclean air") over the aseptic operating field at a uniform velocity (0.3 to 0.5 μm/sec),

sweeping away particles in its path. Laminar airflow can be directed vertically or horizontally, and recirculated air is usually passed through a high efficiency particulate air (HEPA) filter.[302,303] HEPA filters remove particles ≥0.3μm in diameter with an efficiency of 99.97%.[64,300,302,304] Most of the studies examining the efficacy of ultraclean air involve only orthopedic operations.[298,305-311] Charnley and Eftaknan studied vertical laminar airflow systems and exhaust-ventilated clothing and found that their use decreased the SSI rate from 9% to 1%.[305] However, other variables (i.e., surgeon experience and surgical technique) changed at the same time as the type of ventilation, which may have confounded the associations. In a multicenter study examining 8,000 total hip and knee replacements, Lidwell et al. compared the effects of ultraclean air alone, antimicrobial prophylaxis alone, and ultraclean air in combination with antimicrobial prophylaxis on the rate of deep SSIs.[307] The SSI rate following operations in which ultraclean air alone was used decreased from 3.4% to 1.6%, whereas the rate for those who received only antimicrobial prophylaxis decreased from 3.4% to 0.8%. When both interventions were used in combination, the SSI rate decreased from 3.4% to 0.7%. These findings suggest that both ultraclean air and antimicrobial prophylaxis can reduce the incidence of SSI following orthopedic implant operations, but antimicrobial prophylaxis is more beneficial than ultraclean air. Intraoperative UV radiation has not been shown to decrease overall SSI risk.[94,312]

(2) Environmental surfaces

Environmental surfaces in U.S. operating rooms (e.g., tables, floors, walls, ceilings, lights) are rarely implicated as the sources of pathogens important in the development of SSIs. Nevertheless, it is important to perform routine cleaning of these surfaces to reestablish a clean environment after each operation.[180,212,300,302] There are no data to support routine disinfecting of environmental surfaces or equipment between operations in the absence of contamination or visible soiling. When visible soiling of surfaces or equipment occurs during an operation, an Environmental Protection Agency (EPA)-approved hospital disinfectant should be used to decontaminate the affected areas before the next operation.[180,212,300-302,313-315] This is in keeping with the Occupational Safety and Health Administration (OSHA) requirement that all equipment and environmental surfaces be cleaned and decontaminated after contact with blood or other potentially infectious materials.[315] Wet-vacuuming of the floor with an EPA-approved hospital disinfectant is performed routinely after the last operation of the day or night. Care should be taken to ensure that medical equipment left in the operating room be covered so that solutions used during cleaning and disinfecting do not contact sterile devices or equipment.[316] There are no data to support special cleaning procedures or closing of an operating room after a contaminated or dirty operation has been performed.[300,301]

Table 8 Parameters for Operating Room Ventilation, American Institute of Architects, 1996

Temperature	68-73°F, depending on normal ambient temperatures
Relative humidity	30%-60%
Air movement	From "clean to less clean" areas
Air changes	Minimum 15 total air changes per hour Minimum 3 air changes of outdoor air per hour

American Institute of Architects.[299]

Tacky mats placed outside the entrance to an operating room/suite have not been shown to reduce the number of organisms on shoes or stretcher wheels, nor do they reduce the risk of SSI.[1,179,295,301]

(3) Microbiologic sampling

Because there are no standardized parameters by which to compare microbial levels obtained from cultures of ambient air or environmental surfaces in the operating room, routine microbiologic sampling cannot be justified. Such environmental sampling should only be performed as part of an epidemiologic investigation.

(4) Conventional sterilization of surgical instruments

Inadequate sterilization of surgical instruments has resulted in SSI outbreaks.[302,317,318] Surgical instruments can be sterilized by steam under pressure, dry heat, ethylene oxide, or other approved methods. The importance of routinely monitoring the quality of sterilization procedures has been established.[1,180,212,299] Microbial monitoring of steam autoclave performance is necessary and can be accomplished by use of a biological indicator.[212,314,319] Detailed recommendations for sterilization of surgical instruments have been published.[212,314,320,321]

(5) Flash sterilization of surgical instruments

The Association for the Advancement of Medical Instrumentation defines flash sterilization as "the process designated for the steam sterilization of patient care items for immediate use."[321] During any operation, the need for emergency sterilization of equipment may arise (e.g., to reprocess an inadvertently dropped instrument). However, flash sterilization is not intended to be used for either reasons of convenience or as an alternative to purchasing additional instrument sets or to save time. Also, flash sterilization is not recommended for implantable devices(*) because of the potential for serious infections.[314,320,321]

*According to the FDA, an implantable device is a "device that is placed into a surgically or naturally formed cavity of the human body if it is intended to remain there for a period of 30 days or more."[321]

Flash sterilization is not recommended as a routine sterilization method because of the lack of timely biologic indicators to monitor performance, absence of protective packaging following sterilization, possibility for contamination of processed items during transportation to operating rooms, and use of minimal sterilization cycle parameters (i.e., time, temperature, pressure).[319] To address some of these concerns, many hospitals have placed equipment for flash sterilization in close proximity to operating rooms and new biologic indicators that provide results in 1 to 3 hours are now available for flash-sterilized items.[322-325] Nevertheless, flash sterilization should be restricted to its intended purpose until studies are performed that can demonstrate comparability with conventional sterilization methods regarding risk of SSI. Sterilization cycle parameters for flash sterilization are shown in Table 9.

b. Surgical attire and drapes

In this section the term *surgical attire* refers to scrub suits, caps/hoods, shoe covers, masks, gloves, and gowns. Although experimental data show that live microorganisms are shed from hair, exposed skin, and mucous membranes of operating room personnel,[75,181,326-330] few controlled clinical studies have evaluated the relationship between the use of surgical attire and SSI risk. Nevertheless, the use of barriers seems prudent to minimize a patient's exposure to the skin, mucous membranes, or hair of surgical team members, as well as to protect surgical team members from exposure to blood and bloodborne pathogens (e.g., human immunodeficiency virus and hepatitis viruses).

(1) Scrub suits

Surgical team members often wear a uniform called a "scrub suit" that consists of pants and a shirt. Policies for laundering, wearing, covering, and changing scrub suits vary greatly. Some policies restrict the laundering of scrub suits to the facility, while other facilities have policies that allow laundering by employees. There are no well-controlled studies evaluating scrub suit laundering as an SSI risk factor.[331] Some facilities have policies that restrict the wearing of scrub suits to the operating suite, while other facilities allow the wearing of cover gowns over scrub suits when personnel leave the suite. The Association of Operating Room Nurses recommends that scrub suits be changed after they become visibly soiled and that they be laundered only in an approved and monitored laundry facility.[212] Additionally, OSHA regulations require that "if a garment(s) is penetrated by blood or other potentially infectious materials, the garment(s) shall be removed immediately or as soon as feasible."[315]

(2) Masks

The wearing of surgical masks during operations to prevent potential microbial contamination of incisions is a longstanding surgical tradition. However, some studies have raised questions about the efficacy and cost-benefit of surgical masks in reducing SSI risk.[328,332-338] Nevertheless, wearing a mask can be beneficial since it protects the wearer's nose and mouth from inadvertent exposures (i.e., splashes) to blood and other body fluids. OSHA regulations require that masks in combination with protective eyewear, such as goggles or glasses with solid shields, or chin-length face shields be worn whenever splashes, spray, spatter, or droplets of blood or other potentially infectious material may be generated and eye, nose, or mouth contamination can be reasonably anticipated.[315] In addition, a respirator certified by the National Institute for Occupational Safety and Health with protection factor N95 or higher is required when the patient has or is suspected of having infectious tuberculosis.[339]

(3) Surgical caps/hoods and shoe covers

Surgical caps/hoods are inexpensive and reduce contamination of the surgical field by organisms shed from the hair and scalp. SSI outbreaks have occasionally been traced to organisms isolated from the hair or scalp (*S. aureus* and group A *Streptococcus*),[75,76] even when caps were worn by personnel during the operation and in the operating suites.

The use of shoe covers has never been shown to decrease SSI risk or to decrease bacteria counts on the operating room floor.[340,341] Shoe covers may, however, protect surgical team members from exposure to blood and other body fluids during an operation. OSHA regulations require that surgical caps or hoods and shoe covers or boots be worn in situations when gross contamination can reasonably be anticipated (e.g., orthopedic operations, penetrating trauma cases).[315]

(4) Sterile gloves

Sterile gloves are put on after donning sterile gowns. A strong theoretical rationale supports the wearing of sterile gloves by all scrubbed members of the surgical team. Sterile gloves are worn to minimize transmission of microorganisms from the hands of team members to patients and to prevent contamination of team members' hands with patients' blood and body fluids. If the integrity of a glove is compromised (e.g., punctured), it should be changed as promptly as safety permits.[315,342,343] Wearing two pairs of gloves (double-gloving) has been shown to reduce hand contact with patients' blood and body fluids when compared to wearing only a single pair.[344,345]

(5) Gowns and drapes

Sterile surgical gowns and drapes are used to create a barrier between the surgical field and potential sources of bacteria. Gowns are worn by all scrubbed surgical team members and drapes are placed over the

patient. There are limited data that can be used to understand the relationship of gown or drape characteristics with SSI risk. The wide variation in the products and study designs make interpretation of the literature difficult.[329,346-350]

Gowns and drapes are classified as disposable (single use) or reusable (multiple use). Regardless of the material used to manufacture gowns and drapes, these items should be impermeable to liquids and viruses.[351,352] In general, only gowns reinforced with films, coatings, or membranes appear to meet standards developed by the American Society for Testing and Materials.[351-353] However, such "liquid-proof" gowns may be uncomfortable because they also inhibit heat loss and the evaporation of sweat from the wearer's body. These factors should be considered when selecting gowns.[353,354] A discussion of the role of gowns and drapes in preventing the transmission of bloodborne pathogens is beyond the scope of this document.[355]

c. Asepsis and surgical technique

(1) Asepsis

Rigorous adherence to the principles of asepsis by all scrubbed personnel is the foundation of surgical site infection prevention. Others who work in close proximity to the sterile surgical field, such as anesthesia personnel who are separated from the field only by a drape barrier, also must abide by these principles. SSIs have occurred in which anesthesia personnel were implicated as the source of the pathogen.[34,231,234,356-358] Anesthesiologists and nurse anesthetists perform a variety of invasive procedures such as placement of intravascular devices and endotracheal tubes, and administration of intravenous drugs and solutions. Lack of adherence to the principles of asepsis during such procedures,[359] including use of common syringes[360,361] and contaminated infusion pumps,[359,362-364] and the assembly of equipment and solutions in advance of procedures,[316,360] have been associated with outbreaks of postoperative infections, including SSI. Recommendations for infection control practices in anesthesiology have been published.[212,365-367]

(2) Surgical technique

Excellent surgical technique is widely believed to reduce the risk of SSI.[26,49,179,180,368,369] Such techniques include maintaining effective hemostasis while preserving adequate blood supply, preventing hypothermia, gently handling tissues, avoiding inadvertent entries into a hollow viscus, removing devitalized (e.g., necrotic or charred) tissues, using drains and suture material appropriately, eradicating dead space, and appropriately managing the postoperative incision.

Table 9. Parameters for Flash Sterilization Cycles, Association for the Advancement of Medical Instrumentation

	Minimum Exposure Time and Temperature
Gravity-displacement	
Nonporous items	3 min at 132°C (270°F)
Nonporous and porous items	10 min at 132°C (270°F)
Prevacuum	
Nonporous items	3 min at 132°C (270°F)
Nonporous and porous items	4 min at 132°C (270°F)

Association for the Advancement of Medical Instrumentation.[321]

Any foreign body, including suture material, a prosthesis, or drain, may promote inflammation at the surgical site[94] and may increase the probability of SSI after otherwise benign levels of tissue contamination. Extensive research compares different types of suture material and their presumed relationships to SSI risk.[370-379] In general, monofilament sutures appear to have the lowest infection-promoting effects.[3,94,179,180]

A discussion of appropriate surgical drain use and details of drain placement exceed the scope of this document, but general points should be briefly noted. Drains placed through an operative incision increase incisional SSI risk.[380] Many authorities suggest placing drains through a separate incision distant from the operative incision.[283,381] It appears that SSI risk also decreases when closed suction drains are used rather than open drains.[174] Closed suction drains can effectively evacuate postoperative hematomas or seromas, but timing of drain removal is important. Bacterial colonization of initially sterile drain tracts increases with the duration of time the drain is left in place.[382]

Hypothermia in surgical patients, defined as a core body temperature below 36°C, may result from general anesthesia, exposure to cold, or intentional cooling such as is done to protect the myocardium and central nervous system during cardiac operations.[302,383,384] In one study of patients undergoing colorectal operations, hypothermia was associated with an increased SSI risk.[385] Mild hypothermia appears to increase incisional SSI risk by causing vasoconstriction, decreased delivery of oxygen to the wound space, and subsequent impairment of function of phagocytic leukocytes (i.e., neutrophils).[386-390] In animal models, supplemental oxygen administration has been shown to reverse the dysfunction of phagocytes in fresh incisions.[391] In recent human experiments, controlled local heating of incisions with an electrically powered bandage has been shown to improve tissue oxygenation.[392] Randomized clinical trials are needed to establish that measures which improve wound space oxygenation can reduce SSI risk.

4. Operative characteristics: Postoperative issues

a. Incision care

The type of postoperative incision care is determined by whether the incision is closed primarily (i.e., the skin edges are re-approximated at the end of the operation), left open to be closed later, or left open to heal by second intention. When a surgical incision is closed primarily, as most are, the incision is usually covered with a sterile dressing for 24 to 48 hours.[393,394] Beyond 48 hours, it is unclear whether an incision must be covered by a dressing or whether showering or bathing is detrimental to healing. When a surgical incision is left open at the skin level for a few days before it is closed (delayed primary closure), a surgeon has determined that it is likely to be contaminated or that the patient's condition prevents primary closure (e.g., edema at the site). When such is the case, the incision is packed with a sterile dressing. When a surgical incision is left open to heal by second intention, it is also packed with sterile moist gauze and covered with a sterile dressing. The American College of Surgeons, CDC, and others have recommended using sterile gloves and equipment (sterile technique) when changing dressings on any type of surgical incision.[180,395-397]

b. Discharge planning

In current practice, many patients are discharged very soon after their operation, before surgical incisions have fully healed.[398] The lack of optimum protocols for home incision care dictates that much of what is done at home by the patient, family, or home care agency practitioners must be individualized. The intent of discharge planning is to maintain integrity of the healing incision, educate the patient about the signs and symptoms of infection, and advise the patient about whom to contact to report any problems.

F. SSI SURVEILLANCE

Surveillance of SSI with feedback of appropriate data to surgeons has been shown to be an important component of strategies to reduce SSI risk.[16,399,400] A successful surveillance program includes the use of epidemiologically sound infection definitions (Tables 1 and 2) and effective surveillance methods, stratification of SSI rates according to risk factors associated with SSI development, and data feedback.[25]

1. SSI risk stratification

a. Concepts

Three categories of variables have proven to be reliable predictors of SSI risk: (1) those that estimate the intrinsic degree of microbial contamination of the surgical site, (2) those that measure the duration of an operation, and (3) those that serve as markers for host susceptibility.[25] A widely accepted scheme for classifying the degree of intrinsic microbial contamination of a surgical site was developed by the 1964 NAS/NRC Cooperative Research Study and modified in 1982 by CDC for use in SSI surveillance (Table 7).[2,94] In this scheme, a member of the surgical team classifies the patient's wound at the completion of the operation. Because of its ease of use and wide availability, the surgical wound classification has been used to predict SSI risk.[16,94,126,401-405] Some researchers have suggested that surgeons compare clean wound SSI rates with those of other surgeons.[16,399] However, two CDC efforts—the SENIC Project and the NNIS system—incorporated other predictor variables into SSI risk indices. These showed that even within the category of clean wounds, the SSI risk varied by risk category from 1.1% to 15.8% (SENIC) and from 1.0% to 5.4% (NNIS).[125,126] In addition, sometimes an incision is incorrectly classified by a surgical team member or not classified at all, calling into question the reliability of the classification. Therefore, reporting SSI rates stratified by wound class alone is not recommended.

Data on 10 variables collected in the SENIC Project were analyzed by using logistic regression modeling to develop a simple additive SSI risk index.[125] Four of these were found to be independently associated with SSI risk: (1) an abdominal operation, (2) an operation lasting >2 hours, (3) a surgical site with a wound classification of either contaminated or dirty/infected, and 4) an operation performed on a patient having ≥3 discharge diagnoses. Each of these equally weighted factors contributes a point when present, such that the risk index values range from 0 to 4. By using these factors, the SENIC index predicted SSI risk twice as well as the traditional wound classification scheme alone.

The NNIS risk index is operation-specific and applied to prospectively collected surveillance data. The index values range from 0 to 3 points and are defined by three independent and equally weighted variables. One point is scored for each of the following when present: (1) American Society of Anesthesiologists (ASA) Physical Status Classification of >2 (Table 10), (2) either contaminated or dirty/infected wound classification (Table 7), and (3) length of operation >T hours, where T is the approximate 75th percentile of the duration of the specific operation being performed.[126] The ASA class replaced discharge diagnoses of the SENIC risk index as a surrogate for the patient's underlying severity of illness (host susceptibility)[406,407] and has the advantage of being readily available in the chart during the patient's hospital stay. Unlike SENIC's constant 2-hour cut-point for duration of operation, the operation-specific cut-points used in the NNIS risk index increase its discriminatory power compared to the SENIC index.[126]

b. Issues

Adjustment for variables known to confound rate estimates is critical if valid comparisons of SSI rates are to be made between surgeons or hospitals.[408] Risk stratification, as described above, has proven useful for this purpose, but relies on the ability of surveillance personnel to find and record data consistently and correctly. For the three variables used in the NNIS risk index, only one study has focused on how accurately any of them are recorded. Cardo et al. found that surgical team members' accuracy in assessing wound classification for general and trauma surgery was 88% (95% CI: 82%-94%).[409] However, there are sufficient ambiguities in the wound class definitions themselves to warrant concern about the reproducibility of Cardo's results. The accuracy of recording the duration of operation (i.e., time from skin incision to skin closure) and the ASA class has not been studied. In an unpublished report from the NNIS system, there was evidence that overreporting of high ASA class existed in some hospitals. Further validation of the reliability of the recorded risk index variables is needed.

Additionally, the NNIS risk index does not adequately discriminate the SSI risk for all types of operations.[27,410] It seems likely that a combination of risk factors specific to patients undergoing an operation will be more predictive. A few studies have been performed to develop procedure-specific risk indices[218,411-414] and research in this area continues within CDC's NNIS system.

2. SSI surveillance methods

SSI surveillance methods used in both the SENIC Project and the NNIS system were designed for monitoring inpatients at acute-care hospitals. Over the past decade, the shift from inpatient to outpatient surgical care (also called ambulatory or day surgery) has been dramatic. It has been estimated that 75% of all operations in the United States will be performed in outpatient settings by the year 2000.[4] While it may be appropriate to use common definitions of SSI for inpatients and outpatients,[415] the types of operations monitored, the risk factors assessed, and the case-finding methods used may differ. New predictor variables may emerge from analyses of SSIs among outpatient surgery patients, which may lead to different ways of estimating SSI risk in this population.

The choice of which operations to monitor should be made jointly by surgeons and infection control personnel. Most hospitals do not have the resources to monitor all surgical patients all the time, nor is it likely that the same intensity of surveillance is necessary for certain low-risk procedures. Instead, hospitals should target surveillance efforts toward high-risk procedures.[416]

a. Inpatient SSI surveillance

Two methods, alone or together, have been used to identify inpatients with SSIs: (1) direct observation of the surgical site by the surgeon, trained nurse surveyor, or infection control personnel[16,97,399,402,409,417-420] and (2) indirect detection by infection control personnel through review of laboratory reports, patient records, and discussions with primary care providers.[15,84,399,402,404,409,418,421-427] The surgical literature suggests that direct observation of surgical sites is the most accurate method to detect SSIs, although sensitivity data are lacking.[16,399,402,417,418] Much of the SSI data reported in the infection control literature has been generated by indirect case-finding methods,[125,126,422,425,426,428-430] but some studies of direct methods also have been conducted.[97,409] Some studies use both methods of detection.[84,409,424,427,431] A study that focused solely on the sensitivity and specificity of SSIs detected by indirect methods found a sensitivity of 83.8% (95% CI: 75.7%-91.9%) and a specificity of 99.8% (95% CI: 99%-100%).[409] Another study showed that chart review triggered by a computer-generated report of antibiotic orders for post-cesarean section patients had a sensitivity of 89% for detecting endometritis.[432]

Indirect SSI detection can readily be performed by infection control personnel during surveillance rounds. The work includes gathering demographic, infection, surgical, and laboratory data on patients who have undergone operations of interest.[433] These data can be obtained from patients' medical records, including microbiology, histopathology, laboratory, and pharmacy data; radiology reports; and records from the operating room. Additionally, inpatient admissions, emergency room, and clinic visit records are sources of data for those postdischarge surgical patients who are readmitted or seek follow-up care.

The optimum frequency of SSI case-finding by either method is unknown and varies from daily to ≤3 times per week, continuing until the patient is discharged from the hospital. Because duration of hospitalization is often very short, postdischarge SSI surveillance has

Table 10. Physical Status Classification, American Society of Anesthesiologists*

Code	Patient's Preoperative Physical Status
1	Normally healthy patient
2	Patient with mild systemic disease
3	Patient with severe systemic disease that is not incapacitating
4	Patient with an incapacitating systemic disease that is a constant threat to life
5	Moribund patient who is not expected to survive for 24 hours with or without operation

*Reference 406.
Note: The above is the version of the ASA Physical Status Classification System that was current at the time of development of, and still is used in, the NNIS Risk Index. Meanwhile, the American Society of Anesthesiologists has revised their classification system; the most recent version is available at *http://www.asahq.org/profinfo/physical status.html*.

become increasingly important to obtain accurate SSI rates (refer to "Postdischarge SSI Surveillance" section).

To calculate meaningful SSI rates, data must be collected on all patients undergoing the operations of interest (i.e., the population at risk). Because one of its purposes is to develop strategies for risk stratification, the NNIS system collects the following data on all surgical patients surveyed: operation date; NNIS operative procedure category;[434] surgeon identifier; patient identifier; age and sex; duration of operation; wound class; use of general anesthesia; ASA class; emergency; trauma; multiple procedures; endoscopic approach; and discharge date.[433] With the exception of discharge date, these data can be obtained manually from operating room logs or be electronically downloaded into surveillance software, thereby substantially reducing manual transcription and data entry errors.[433] Depending on the needs for risk-stratified SSI rates by personnel in infection control, surgery, and quality assurance, not all data elements may be pertinent for every type of operation. At minimum, however, variables found to be predictive of increased SSI risk should be collected (refer to "SSI Risk Stratification" section).

b. Postdischarge SSI surveillance

Between 12% and 84% of SSIs are detected after patients are discharged from the hospital.[98,337,402,428,435-454] At least two studies have shown that most SSIs become evident within 21 days after operation.[446,447] Since the length of postoperative hospitalization continues to decrease, many SSIs may not be detected for several weeks after discharge and may not require readmission to the operating hospital. Dependence solely on inpatient case-finding will result in underestimates of SSI rates for some operations (e.g., coronary artery bypass graft) (CDC/NNIS system, unpublished data, 1998). Any comparison of SSI rates must take into account whether case-finding included SSIs detected after discharge. For comparisons to be valid, even in the same institution over time, the postdischarge surveillance methods must be the same.

Postdischarge surveillance methods have been used with varying degrees of success for different procedures and among hospitals and include (1) direct examination of patients' wounds during follow-up visits to either surgery clinics or physicians' offices,[150,399,402,404,430,436,440,441,447,452,455] (2) review of medical records of surgery clinic patients,[404,430,439] (3) patient surveys by mail or telephone,[435,437,438,441,442,444,445,448,449,455-457] or (4) surgeon surveys by mail or telephone.[98,428,430,437-439,443,444,446,448,450,451,455] One study found that patients have difficulty assessing their own wounds for infection (52% specificity, 26% positive predictive value),[458] suggesting that data obtained by patient questionnaire may inaccurately represent actual SSI rates.

Recently, Sands et al. performed a computerized search of three databases to determine which best identified SSIs: ambulatory encounter records for diagnostic, testing, and treatment codes; pharmacy records for specific antimicrobial prescriptions; and administrative records for rehospitalizations and emergency room visits.[446] This study found that pharmacy records indicating a patient had received antimicrobial agents commonly used to treat soft tissue infections had the highest sensitivity (50%) and positive predictive value (19%), although even this approach alone was not very effective.

As integrated health information systems expand, tracking surgical patients through the entire course of care may become more feasible, practical, and effective. At this time, no consensus exists on which postdischarge surveillance methods are the most sensitive, specific, and practical. Methods chosen will necessarily reflect the hospital's unique mix of operations, personnel resources, and data needs.

c. Outpatient SSI surveillance

Both direct and indirect methods have been used to detect SSIs that complicate outpatient operations. One 8-year study of operations for hernia and varicose veins used home visits by district health nurses combined with a survey completed by the surgeon at the patient's 2-week postoperative clinic visit to identify SSIs.[459] While ascertainment was essentially 100%, this method is impractical for widespread implementation. High response rates have been obtained from questionnaires mailed to surgeons (72%->90%).[443,444,446,455,459-461] Response rates from telephone questionnaires administered to patients were more variable (38%,[444] 81%,[457] and 85%[455]), and response rates from questionnaires mailed to patients were quite low (15%[455] and 33%[446]). At this time, no single detection method can be recommended. Available resources and data needs determine which method(s) should be used and which operations should be monitored. Regardless of which detection method is used, it is recommended that the CDC NNIS definitions of SSI (Tables 1 and 2) be used without modification in the outpatient setting.

G. GUIDELINE EVALUATION PROCESS

The value of the HICPAC guidelines is determined by those who use them. To help assess that value, HICPAC is developing an evaluation tool to learn how guidelines meet user expectations, and how and when these guidelines are disseminated and implemented.

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II. Recommendations for prevention of surgical site infection

A. RATIONALE

The Guideline for Prevention of Surgical Site Infection, 1999, provides recommendations concerning reduction of surgical site infection risk. Each recommendation is categorized on the basis of existing scientific data, theoretical rationale, and applicability. However, the previous CDC system for categorizing recommendations has been modified slightly.

Category I recommendations, including IA and IB, are those recommendations that are viewed as effective by HICPAC and experts in the fields of surgery, infectious diseases, and infection control. Both Category IA and IB recommendations are applicable for, and should be adopted by, all healthcare facilities; IA and IB recommendations differ only in the strength of the supporting scientific evidence.

Category II recommendations are supported by less scientific data than Category I recommendations; such recommendations may be appropriate for addressing specific nosocomial problems or specific patient populations.

No recommendation is offered for some practices, either because there is a lack of consensus regarding their efficacy or because the available scientific evidence is insufficient to support their adoption. For such unresolved issues, practitioners should use judgement to determine a policy regarding these practices within their organization. Recommendations that are based on federal regulation are denoted with an asterisk.

B. RANKINGS

Category IA. Strongly recommended for implementation and supported by well-designed experimental, clinical, or epidemiological studies.

Category IB. Strongly recommended for implementation and supported by some experimental, clinical, or epidemiological studies and strong theoretical rationale.

Category II. Suggested for implementation and supported by suggestive clinical or epidemiological studies or theoretical rationale.

No recommendation; unresolved issue. Practices for which insufficient evidence or no consensus regarding efficacy exists.

Practices required by federal regulation are denoted with an asterisk (*).

C. RECOMMENDATIONS

1. Preoperative

a. Preparation of the patient

1. Whenever possible, identify and treat all infections remote to the surgical site before elective operation and postpone elective operations on patients with remote site infections until the infection has resolved. *Category IA*
2. Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation. *Category IA*
3. If hair is removed, remove immediately before the operation, preferably with electric clippers. *Category IA*
4. Adequately control serum blood glucose levels in all diabetic patients and particularly avoid hyperglycemia perioperatively. *Category IB*
5. Encourage tobacco cessation. At minimum, instruct patients to abstain for at least 30 days before elective operation from smoking cigarettes, cigars, pipes, or any other form of tobacco consumption (e.g., chewing/dipping). *Category IB*
6. Do not withhold necessary blood products from surgical patients as a means to prevent SSI. *Category IB*
7. Require patients to shower or bathe with an antiseptic agent on at least the night before the operative day. *Category IB*
8. Thoroughly wash and clean at and around the incision site to remove gross contamination before performing antiseptic skin preparation. *Category IB*
9. Use an appropriate antiseptic agent for skin preparation (Table 6). *Category IB*
10. Apply preoperative antiseptic skin preparation in concentric circles moving toward the periphery. The prepared area must be large enough to extend the incision or create new incisions or drain sites, if necessary. *Category II*
11. Keep preoperative hospital stay as short as possible while allowing for adequate preoperative preparation of the patient. *Category II*
12. No recommendation to taper or discontinue systemic steroid use (when medically permissible) before elective operation. *Unresolved issue*

13. No recommendation to enhance nutritional support for surgical patients solely as a means to prevent SSI. *Unresolved issue*
14. No recommendation to preoperatively apply mupirocin to nares to prevent SSI. *Unresolved issue*
15. No recommendation to provide measures that enhance wound space oxygenation to prevent SSI. *Unresolved issue*

b. Hand/forearm antisepsis for surgical team members

1. Keep nails short and do not wear artificial nails. *Category IB*
2. Perform a preoperative surgical scrub for at least 2 to 5 minutes using an appropriate antiseptic (Table 6). Scrub the hands and forearms up to the elbows. *Category IB*
3. After performing the surgical scrub, keep hands up and away from the body (elbows in flexed position) so that water runs from the tips of the fingers toward the elbows. Dry hands with a sterile towel and don a sterile gown and gloves. *Category IB*
4. Clean underneath each fingernail prior to performing the first surgical scrub of the day. *Category II*
5. Do not wear hand or arm jewelry. *Category II*
6. No recommendation on wearing nail polish. *Unresolved Issue*

c. Management of infected or colonized surgical personnel

1. Educate and encourage surgical personnel who have signs and symptoms of a transmissible infectious illness to report conditions promptly to their supervisory and occupational health service personnel. *Category IB*
2. Develop well-defined policies concerning patient-care responsibilities when personnel have potentially transmissible infectious conditions. These policies should govern (a) personnel responsibility in using the health service and reporting illness, (b) work restrictions, and (c) clearance to resume work after an illness that required work restriction. The policies also should identify persons who have the authority to remove personnel from duty. *Category IB*
3. Obtain appropriate cultures from, and exclude from duty, surgical personnel who have draining skin lesions until infection has been ruled out or personnel have received adequate therapy and infection has resolved. *Category IB*
4. Do not routinely exclude surgical personnel who are colonized with organisms such as *S. aureus* (nose, hands, or other body site) or group A *Streptococcus*, unless such personnel have been linked epidemiologically to dissemination of the organism in the healthcare setting. *Category IB*

d. Antimicrobial prophylaxis

1. Administer a prophylactic antimicrobial agent only when indicated, and select it based on its efficacy against the most common pathogens causing SSI for a specific operation (Table 4) and published recommendations.[266,268,269,282-284] *Category IA*
2. Administer by the intravenous route the initial dose of prophylactic antimicrobial agent, timed such that a bactericidal concentration of the drug is established in serum and tissues when the incision is made. Maintain therapeutic levels of the agent in serum and tissues throughout the operation and until, at most, a few hours after the incision is closed in the operating room. *Category IA*
3. Before elective colorectal operations in addition to d2 above, mechanically prepare the colon by use of enemas and cathartic agents. Administer nonabsorbable oral antimicrobial agents in divided doses on the day before the operation. *Category IA*
4. For high-risk cesarean section, administer the prophylactic antimicrobial agent immediately after the umbilical cord is clamped. *Category IA*
5. Do not routinely use vancomycin for antimicrobial prophylaxis. *Category IB*

2. Intraoperative

a. Ventilation

1. Maintain positive-pressure ventilation in the operating room with respect to the corridors and adjacent areas. *Category IB*
2. Maintain a minimum of 15 air changes per hour, of which at least 3 should be fresh air. *Category IB*
3. Filter all air, recirculated and fresh, through the appropriate filters per the American Institute of Architects' recommendations.[299] *Category IB*
4. Introduce all air at the ceiling, and exhaust near the floor. *Category IB*
5. Do not use UV radiation in the operating room to prevent SSI. *Category IB*
6. Keep operating room doors closed except as needed for passage of equipment, personnel, and the patient. *Category IB*
7. Consider performing orthopedic implant operations in operating rooms supplied with ultraclean air. *Category II*
8. Limit the number of personnel entering the operating room to necessary personnel. *Category II*

b. Cleaning and disinfection of environmental surfaces

1. When visible soiling or contamination with blood or other body fluids of surfaces or equipment occurs during an operation, use an EPA-approved hospital disinfectant to clean the affected areas before the next operation. *Category IB**

2. Do not perform special cleaning or closing of operating rooms after contaminated or dirty operations. *Category IB*
3. Do not use tacky mats at the entrance to the operating room suite or individual operating rooms for infection control. *Category IB*
4. Wet vacuum the operating room floor after the last operation of the day or night with an EPA-approved hospital disinfectant. *Category II*
5. No recommendation on disinfecting environmental surfaces or equipment used in operating rooms between operations in the absence of visible soiling. *Unresolved issue*

c. Microbiologic sampling

1. Do not perform routine environmental sampling of the operating room. Perform microbiologic sampling of operating room environmental surfaces or air only as part of an epidemiologic investigation. *Category IB*

d. Sterilization of surgical instruments

1. Sterilize all surgical instruments according to published guidelines.[212,299,314,321] *Category IB*
2. Perform flash sterilization only for patient care items that will be used immediately (e.g., to reprocess an inadvertently dropped instrument). Do not use flash sterilization for reasons of convenience, as an alternative to purchasing additional instrument sets, or to save time. *Category IB*

e. Surgical attire and drapes

1. Wear a surgical mask that fully covers the mouth and nose when entering the operating room if an operation is about to begin or already under way, or if sterile instruments are exposed. Wear the mask throughout the operation. *Category IB**
2. Wear a cap or hood to fully cover hair on the head and face when entering the operating room. *Category IB**
3. Do not wear shoe covers for the prevention of SSI. *Category IB**
4. Wear sterile gloves if a scrubbed surgical team member. Put on gloves after donning a sterile gown. *Category IB**
5. Use surgical gowns and drapes that are effective barriers when wet (i.e., materials that resist liquid penetration). *Category IB*
6. Change scrub suits that are visibly soiled, contaminated, and/or penetrated by blood or other potentially infectious materials. *Category IB**
7. No recommendations on how or where to launder scrub suits, on restricting use of scrub suits to the operating suite, or for covering scrub suits when out of the operating suite. *Unresolved issue*

f. Asepsis and surgical technique

*Federal regulation: OSHA

1. Adhere to principles of asepsis when placing intravascular devices (e.g., central venous catheters), spinal or epidural anesthesia catheters, or when dispensing and administering intravenous drugs. *Category IA*
2. Assemble sterile equipment and solutions immediately prior to use. *Category II*
3. Handle tissue gently, maintain effective hemostasis, minimize devitalized tissue and foreign bodies (i.e., sutures, charred tissues, necrotic debris), and eradicate dead space at the surgical site. *Category IB*
4. Use delayed primary skin closure or leave an incision open to heal by second intention if the surgeon considers the surgical site to be heavily contaminated (e.g., Class III and Class IV). *Category IB*
5. If drainage is necessary, use a closed suction drain. Place a drain through a separate incision distant from the operative incision. Remove the drain as soon as possible. *Category IB*

3. Postoperative incision care

a. Protect with a sterile dressing for 24 to 48 hours postoperatively an incision that has been closed primarily. *Category IB*
b. Wash hands before and after dressing changes and any contact with the surgical site. *Category IB*
c. When an incision dressing must be changed, use sterile technique. *Category II*
d. Educate the patient and family regarding proper incision care, symptoms of SSI, and the need to report such symptoms. *Category II*
e. No recommendation to cover an incision closed primarily beyond 48 hours, nor on the appropriate time to shower or bathe with an uncovered incision. *Unresolved Issue*

4. Surveillance

a. Use CDC definitions of SSI (Table 1) without modification for identifying SSI among surgical inpatients and outpatients. *Category IB*
b. For inpatient case-finding (including readmissions), use direct prospective observation, indirect prospective detection, or a combination of both direct and indirect methods for the duration of the patient's hospitalization. *Category IB*
c. When postdischarge surveillance is performed for detecting SSI following certain operations (e.g., coronary artery bypass graft), use a method that accommodates available resources and data needs. *Category II*
d. For outpatient case-finding, use a method that accommodates available resources and data needs. *Category IB*
e. Assign the surgical wound classification upon

completion of an operation. A surgical team member should make the assignment. *Category II*

f. For each patient undergoing an operation chosen for surveillance, record those variables shown to be associated with increased SSI risk (e.g., surgical wound class, ASA class, and duration of operation). *Category IB*

g. Periodically calculate operation-specific SSI rates stratified by variables shown to be associated with increased SSI risk (e.g., NNIS risk index). *Category IB*

h. Report appropriately stratified, operation-specific SSI rates to surgical team members. The optimum frequency and format for such rate computations will be determined by stratified case-load sizes (denominators) and the objectives of local, continuous quality improvement initiatives. *Category IB*

i. No recommendation to make available to the infection control committee coded surgeon-specific data. *Unresolved issue*

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References

1. Garner JS. CDC guideline for prevention of surgical wound infections, 1985. Supercedes guideline for prevention of surgical wound infections published in 1982. (Originally published in 1995). Revised. Infect Control 1986;7(3):193-200.
2. Simmons BP. Guideline for prevention of surgical wound infections. Infect Control 1982;3:185-196.
3. Garner JS. The CDC Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1993;21:160-2.
4. Hecht AD. Creating greater efficiency in ambulatory surgery. J Clin Anesth 1995;7:581-4.
5. Horwitz JR, Chwals WJ, Doski JJ, Suescun EA, Cheu HW, Lally KP. Pediatric wound infections: a prospective multicenter study. Ann Surg 1998;227:553-8.
6. Golub R, Siddiqui F, Pohl D. Laparoscopic versus open appendectomy: a metaanalysis. J Am Coll Surg 1998;186:545-53.
7. Mayol J, Garcia-Aguilar J, Ortiz-Oshiro E, De-Diego Carmona JA, Ferndandez-Represa JA. Risks of the minimal access approach for laparoscopic surgery: multivariate analysis of morbidity related to umbilical trocar insertion. World J Surg 1997;21:529-33.
8. Lacy AM, Garcia-Valdecasas JC, Delgado S, Grande L, Fuster J, Tabet J, et al. Postoperative complications of laparoscopic-assisted colectomy. Surg Endosc 1997;11:119-22.
9. Pagni S, Salloum EJ, Tobin GR, VanHimbergen DJ, Spence PA. Serious wound infections after minimally invasive coronary bypass procedures. Ann Thorac Surg 1998;66:92-4.
10. The Southern Surgeons Club. A prospective analysis of 1518 laparoscopic cholecystectomies. N Engl J Med 1991;324:1073-8.
11. Centers for Disease Control and Prevention. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986-April 1997, issued May 1997. Am J Infect Control 1997;25:477-87.
12. Food and Drug Administration. Topical antimicrobial drug products for over-the-counter human use: tentative final monograph for health-care antiseptic drug products—proposed rule (21 CFR Parts 333 and 369). Federal Register 1994; 59:31441-52.
13. Centers for Disease Control and Prevention, National Center for Health Statistics. Vital and Health Statistics, Detailed Diagnoses and Procedures, National Hospital Discharge Survey, 1994. Vol 127. Hyattsville, Maryland: DHHS Publication; 1997.
14. Emori TG, Gaynes RP. An overview of nosocomial infections, including the role of the microbiology laboratory. Clin Microbiol Rev 1993;6(4):428-42.
15. Cruse P. Wound infection surveillance. Rev Infect Dis 1981;4(3):734-7.
16. Cruse PJ, Foord R. The epidemiology of wound infection: a 10-year prospective study of 62,939 wounds. Surg Clin North Am 1980;60(1):27-40.
17. Martone WJ, Jarvis WR, Culver DH, Haley RW. Incidence and nature of endemic and epidemic nosocomial infections. In: Bennett JV, Brachman PS, eds. Hospital Infections. 3rd ed. Boston: Little, Brown and Co; 1992. p. 577-96.
18. Boyce JM, Potter-Bynoe G, Dziobek L. Hospital reimbursement patterns among patients with surgical wound infections following open heart surgery. Infect Control Hosp Epidemiol 1990;11(2):89-93.
19. Poulsen KB, Bremmelgaard A, Sorensen AI, Raahave D, Petersen JV. Estimated costs of postoperative wound infections. A case-control study of marginal hospital and social security costs. Epidemiol Infect 1994;113(2):283-95.
20. Vegas AA, Jodra VM, Garcia ML. Nosocomial infection in surgery wards: a controlled study of increased duration of hospital stays and direct cost of hospitalization. Eur J Epidemiol 1993;9(5):504-10.
21. Albers BA, Patka P, Haarman HJ, Kostense PJ. Cost effectiveness of preventive antibiotic administration for lowering risk of infection by 0.25%. [German]. Unfallchirurg 1994;97(12):625-8.
22. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Infect Control Hosp Epidemiol 1992;13(10):606-8.
23. Ehrenkranz NJ, Richter EI, Phillips PM, Shultz JM. An apparent excess of operative site infections: analyses to evaluate false-positive diagnoses. Infect Control Hosp Epidemiol 1995;16(12):712-6.
24. Taylor G, McKenzie M, Kirkland T, Wiens R. Effect of surgeon's diagnosis on surgical wound infection rates. Am J Infect Control 1990;18(5):295-9.
25. SHEA, APIC, CDC, SIS. Consensus paper on the surveillance of surgical wound infections. Infect Control Hosp Epidemiol 1992;13(10):599-605.
26. Nooyen SM, Overbeek BP, Brutel de la Riviere A, Storm AJ, Langemeyer JM. Prospective randomised comparison of single-dose versus multiple-dose cefuroxime for prophylaxis in coronary artery bypass grafting. Eur J Clin Microbiol Infect Dis 1994;13:1033-7.
27. Centers for Disease Control and Prevention. National Nosocomial Infections Surveillance (NNIS) report, data summary from October 1986-April 1996, issued May 1996. A report from the National Nosocomial Infections Surveillance (NNIS) System. Am J Infect Control 1996;24:380-8.

28. Schaberg DR. Resistant gram-positive organisms. Ann Emerg Med 1994;24(3):462-4.
29. Schaberg DR, Culver DH, Gaynes RP. Major trends in the microbial etiology of nosocomial infection. Am J Med 1991;91(3B):72S-5S.
30. Jarvis WR. Epidemiology of nosocomial fungal infections, with emphasis on *Candida* species. Clin Infect Dis 1995;20:1526-30.
31. Centers for Disease Control. Nosocomial outbreak of *Rhizopus* infections associated with Elastoplast wound dressings—Minnesota. MMWR 1978;27:33-4.
32. Pearson RD, Valenti WM, Steigbigel RT. *Clostridium perfringens* wound infections associated with elastic bandages. JAMA 1980;244:1128-30.
33. Richet HM, Craven PC, Brown JM, Lasker BA, Cox CD, McNeil MM, et al. A cluster of *Rhodococcus (Gordona) bronchialis* sternal-wound infections after coronary-artery bypass surgery. N Engl J Med 1991;324:104-9.
34. Wenger PN, Brown JM, McNeil MM, Jarvis WR. *Nocardia farcinica* sternotomy site infections in patients following open heart surgery. J Infect Dis 1998;178:1539-43.
35. Lowry PW, Blankenship RJ, Gridley W, Troup NJ, Tompkins LS. A cluster of *Legionella* sternal-wound infections due to postoperative topical exposure to contaminated tap water. N Engl J Med 1991;324:109-13.
36. Bassett DC, Stokes KJ, Thomas WR. Wound infection with *Pseudomonas multivorans:* a water-borne contaminant of disinfectant solutions. Lancet 1970;1:1188-91.
37. Cruse PJ. Surgical wound infection. In: Wonsiewicz MJ, ed. Infectious Diseases. Philadelphia: W.B.Saunders Co; 1992. p. 758-64.
38. Altemeier WA, Culbertson WR. Surgical infection. In: Moyer CA, Rhoads JE, Allen JG, Harkins HN, eds. Surgery, principles and practice. 3rd ed. Philadelphia: JB Lippincott; 1965. p. 51-77.
39. Krizek TJ, Robson MC. Evolution of quantitative bacteriology in wound management. Am J Surg 1975;130:579-84.
40. Elek SD, Conen PE. The virulence of *Staphylococcus pyogenes* for man: a study of problems with wound infection. Br J Exp Pathol 1957;38:573-86.
41. Noble WC. The production of subcutaneous staphylococcal skin lesions in mice. Br J Exp Pathol 1965;46:254-62.
42. James RC, MacLeod CJ. Induction of staphylococcal infections in mice with small inocula introduced on sutures. Br J Exp Pathol 1961;42:266-77.
43. Henderson B, Poole S, Wilson M. Microbial/host interactions in health and disease: who controls the cytokine network? Immunopharmacology 1996;35:1-21.
44. Morrison DC, Ryan JL. Endotoxins and disease mechanisms. Ann Rev Med 1987;38:417-32.
45. Demling R, LaLonde C, Saldinger P, Knox J. Multiple-organ dysfunction in the surgical patient: pathophysiology, prevention, and treatment. Curr Probl Surg 1993;30:345-414.
46. Eiseman B, Beart R, Norton L. Multiple organ failure. Surg Gynecol Obstet 1977;14:323-6.
47. Fry DE, Pearlstein L, Fulton RL, Polk HC, Jr. Multiple system organ failure: the role of uncontrolled infection. Arch Surg 1980;115:136-40.
48. Kasper DL. Bacterial capsule—old dogmas and new tricks. J Infect Dis 1986;153:407-15.
49. Dellinger EP. Surgical infections and choice of antibiotics. In: Sabiston DC, ed. Textbook of Surgery. The Biological Basis of Modern Surgical Practice. 15 ed. Philadelphia: W.B.Saunders Co; 1997. p. 264-80.
50. Goeau-Brissonniere O, Leport C, Guidoin R, Lebrault C, Pechere JC, Bacourt F. Experimental colonization of an expanded polytetrafluoroethylene vascular graft with *Staphylococcus aureus*: a quantitative and morphologic study. J Vasc Surg 1987;5(5):743-8.
51. Bergamini TM, Corpus RA Jr., Brittian KR, Peyton JC, Cheadle WG. The natural history of bacterial biofilm graft infection. J Surg Res 1994;56:393-6.
52. Baddour LM, Christensen GD, Hester MG, Bisno AL. Production of experimental endocarditis by coagulase-negative staphylococci: variability in species virulence. J Infect Dis 1984;150:721-7.
53. Christensen GD, Baddour LM, Simpson WA. Phenotypic variation of *Staphylococcus epidermidis* slime production in vitro and in vivo. Infect Immun 1987;55:2870-7.
54. Mayberry-Carson KJ, Tober-Meyer B, Smith JK, Lambe DW Jr., Costerton JW. Bacterial adherence and glycocalyx formation in osteomyelitis experimentally induced with *Staphylococcus aureus*. Infect Immun 1984;43:825-33.
55. Mills J, Pulliam L, Dall L, Marzouk J, Wilson W, Costerton JW. Exopolysaccharide production by *viridans streptococci* in experimental endocarditis. Infect Immun 1984;43:359-67.
56. Kaebnick HW, Bandyk DF, Bergamini TM, Towne JB. The microbiology of explanted vascular prostheses. Surgery 1987;102:756-61.
57. Altemeier WA, Culbertson WR, Hummel RP. Surgical considerations of endogenous infections—sources, types, and methods of control. Surg Clin North Am 1968;48:227-40.
58. Wiley AM, Ha'eri GB. Routes of infection: a study of using "tracer particles" in the orthopedic operating room. Clin Orthop 1979;139:150-5.
59. Slaughter L, Morris JE, Starr A. Prosthetic valvular endocarditis. A 12-year review. Circulation 1973;47:1319-26.
60. Carlsson AK, Lidgren L, Lindberg L. Prophylactic antibiotics against early and late deep infections after total hip replacements. Acta Orthop Scand 1977;48:405-10.
61. Hunter JG, Padilla M, Cooper-Vastola S. Late *Clostridium perfringens* breast implant infection after dental treatment. Ann Plast Surg 1996;36(3):309-12.
62. Stuesse DC, Robinson JH, Durzinsky DS. A late sternal wound infection caused by hematogenous spread of bacteria. Chest 1995;108(6):1742-3.
63. Howe CW. Experimental wound sepsis from transient *Escherichia coli* bacteremia. Surgery 1969;66:570-4.
64. Velasco E, Thuler LC, Martins CA, Dias LM, Conalves VM. Risk factors for infectious complications after abdominal surgery for malignant disease. Am J Infect Control 1996;24(1):1-6.
65. Bruun JN. Post-operative wound infection. Predisposing factors and the effect of a reduction in the dissemination of staphylococci. Acta Med Scand Suppl 1970;514(Suppl):3-89.
66. Simchen E, Rozin R, Wax Y. The Israeli Study of Surgical Infection of drains and the risk of wound infection in operations for hernia. Surg Gynecol Obstet 1990;170:331-7.
67. Edwards LD. The epidemiology of 2056 remote site infections and 1966 surgical wound infections occurring in 1865 patients: a four year study of 40,923 operations at Rush-Presbyterian-St. Luke's Hospital, Chicago. Ann Surg 1976;184:758-66.
68. Valentine RJ, Weigelt JA, Dryer D, Rodgers C. Effect of remote infections on clean wound infection rates. Am J Infect Control 1986;14:64-7.
69. Cioffi GA, Terezhalmy GT, Taybos GM. Total joint replacement: a consideration for antimicrobial prophylaxis. Oral Surg Oral Med Oral Pathol 1988;66(1):124-9.
70. Heggeness MH, Esses SI, Errico T, Yuan HA. Late infection of spinal instrumentation by hematogenous seeding. Spine 1993;18(4):492-6.
71. Mont MA, Waldman B, Banerjee C, Pacheco IH, Hungerford DS. Multiple irrigation, debridement, and retention of components in infected total knee arthroplasty. J Arthroplasty 1997;12(4):426-33.
72. Ozuna RM, Delamarter RB. Pyogenic vertebral osteomyelitis and postsurgical disc space infections. Ortho Clin North Am 1996;27(1):87-94.

73. Schmalzried TP, Amstutz HC, Au MK, Dorey FJ. Etiology of deep sepsis in total hip arthroplasty. The significance of hematogenous and recurrent infections. Clin Orthop 1992;280:200-7.
74. Calia FM, Wolinsky E, Mortimer EA Jr., Abrams JS, Rammelkamp CH Jr. Importance of the carrier state as a source of *Staphylococcus aureus* in wound sepsis. J Hyg (Lond) 1969;67:49-57.
75. Dineen P, Drusin L. Epidemics of postoperative wound infections associated with hair carriers. Lancet 1973;2(7839):1157-9.
76. Mastro TD, Farley TA, Elliott JA, Facklam RR, Perks JR, Hadler JL, et al. An outbreak of surgical-wound infections due to group A *streptococcus* carried on the scalp. N Engl J Med 1990;323:968-72.
77. Ford CR, Peterson DE, Mitchell CR. An appraisal of the role of surgical face masks. Am J Surg 1967;113:787-90.
78. Letts RM, Doermer E. Conversation in the operating theater as a cause of airborne bacterial contamination. J Bone Joint Surg [Am] 1983;65:357-62.
79. Giamarellou H, Antoniadou A. Epidemiology, diagnosis, and therapy of fungal infections in surgery. Infect Control Hosp Epidemiol 1996;17(8):558-64.
80. Lee JT. Surgical wound infections: surveillance for quality improvement. In: Fry DE, ed. Surgical Infections. Boston: Little, Brown and Co; 1995. p. 145-59.
81. Perl TM, Golub JE. New approaches to reduce *Staphylococcus aureus* nosocomial infection rates: treating *S. aureus* nasal carriage. Ann Pharmacother 1998;32:S7-S16.
82. Kluytmans JA, Mouton JW, Ijzerman EP, Vandenbroucke-Grauls CM, Maat AW, Wagenvoort JH, et al. Nasal carriage of *Staphylococcus aureus* as a major risk factor for wound infections after cardiac surgery. J Infect Dis 1995;171:216-9.
83. Perl TM, Cullen JJ, Pfaller MA, Wenzel RP, Herwaldt LA, The MARS Study Team. A randomized, double-blind, placebo-controlled clinical trial of intranasal mupirocin ointment (IM) for prevention of *S. aureus* surgical site infections (SSI) [abstract]. Abstracts of the IDSA 36th Annual Meeting 1998;91(88).
84. Gil-Egea MJ, Pi-Sunyer MT, Verdaguer A, Sanz F, Sitges-Serra A, Eleizegui LT. Surgical wound infections: prospective study of 4,486 clean wounds. Infect Control 1987;8(7):277-80.
85. Nagachinta T, Stephens M, Reitz B, Polk BF. Risk factors for surgical-wound infection following cardiac surgery. J Infect Dis 1987;156:967-73.
86. Lilienfeld DE, Vlahov D, Tenney JH, McLaughlin JS. Obesity and diabetes as risk factors for postoperative wound infections after cardiac surgery. Am J Infect Control 1988;16:3-6.
87. Slaughter MS, Olson MM, Lee JT Jr., Ward HB. A fifteen-year wound surveillance study after coronary artery bypass. Ann Thorac Surg 1993;56(5):1063-8.
88. Bryan AJ, Lamarra M, Angelini GD, West RR, Breckenridge IM. Median sternotomy wound dehiscence: a retrospective case control study of risk factors and outcome. J R Coll Surg Edinb 1992;37:305-8.
89. Jones JK, Triplett RG. The relationship of cigarette smoking to impaired intraoral wound healing: a review of evidence and implications for patient care. J Oral Maxillofac Surg 1992;50(3):237-9; discussion 239-40.
90. Vinton AL, Traverso LW, Jolly PC. Wound complications after modified radical mastectomy compared with tylectomy with axillary lymph node dissection. Am J Surg 1991;161(5):584-8.
91. Holley DT, Toursarkissian B, Vansconez HC, Wells MD, Kenady DE, Sloan DA. The ramifications of immediate reconstruction in the management of breast cancer. Am Surg 1995;61(1):60-5.
92. Beitsch P, Balch C. Operative morbidity and risk factor assessment in melanoma patients undergoing inguinal lymph node dissection. Am J Surg 1992;164(5):462-6; discussion 465-6.
93. Post S, Betzler M, vonDitfurth B, Schurmann G, Kuppers P, Herfarth C. Risks of intestinal anastomoses in Crohn's disease. Ann Surg 1991;213(1):37-42.
94. B'erard F, Gandon J. Postoperative wound infections: the influence of ultraviolet irradiation of the operating room and of various other factors. Ann Surg 1964;160(Suppl 1):1-192.
95. Nystrom PO, Jonstam A, Hojer H, Ling L. Incisional infection after colorectal surgery in obese patients. Acta Chir Scand 1987;153:225-7.
96. He GW, Ryan WH, Acuff TE, Bowman RT, Douthit MB, Yang CQ, et al. Risk factors for operative mortality and sternal wound infection in bilateral internal mammary artery grafting. J Thorac Cardiovasc Surg 1994;107(1):196-202.
97. Barber GR, Miransky J, Brown AE, Coit DG, Lewis FM, Thaler HT, et al. Direct observations of surgical wound infections at a comprehensive cancer center. Arch Surg 1995;130(10):1042-7.
98. Cruse PJ, Foord R. A five-year prospective study of 23,649 surgical wounds. Arch Surg 1973;107:206-10.
99. Claesson BE, Holmlund DE. Predictors of intraoperative bacterial contamination and postoperative infection in elective colorectal surgery. J Hosp Infect 1988;11:127-35.
100. Mishriki SF, Law DJ, Jeffery PJ. Factors affecting the incidence of postoperative wound infection. J Hosp Infect 1990;16:223-30.
101. Doig CM, Wilkinson AW. Wound infection in a children's hospital. Br J Surg 1976;63:647-50.
102. Sharma LK, Sharma PK. Postoperative wound infection in a pediatric surgical service. J Pediatr Surg 1986;21:889-91.
103. Casey J, Flinn WR, Yao JS, Fahey V, Pawlowski J, Bergan JJ. Correlation of immune and nutritional status with wound complications in patients undergoing vascular operations. Surgery 1983;93(6):822-7.
104. Greene KA, Wilde AH, Stulberg BN. Preoperative nutritional status of total joint patients. Relationship to postoperative wound complications. J Arthroplasty 1991;6(4):321-5.
105. Weber TR. A prospective analysis of factors influencing outcome after fundoplication. J Pediatr Surg 1995;30(7):1061-3; discussion 1063-4.
106. Vamvakas EC, Carven JH. Transfusion of white-cell-containing allogeneic blood components and postoperative wound infection: effect of confounding factors. Transfus Med 1998;8:29-36.
107. Vamvakas EC, Carven JH, Hibberd PL. Blood transfusion and infection after colorectal cancer surgery. Transfusion 1996;36:1000-8.
108. Jensen LS, Kissmeyer-Nielsen P, Wolff B, Qvist N. Randomised comparison of leucocyte-depleted versus buffy-coat-poor blood transfusion and complications after colorectal surgery. Lancet 1996;348:841-5.
109. Heiss MM, Mempel W, Jauch KW, Delanoff C, Mayer G, Mempel M, et al. Beneficial effect of autologous blood transfusion on infectious complications after colorectal cancer surgery. Lancet 1993;342:1328-33.
110. Lidgren L. Postoperative orthopaedic infections in patients with diabetes mellitus. Acta Orthop Scand 1973;44:149-51.
111. Gordon SM, Serkey JM, Barr C, Cosgrove D, Potts W. The relationship between glycosylated hemoglobin (HgA1c) levels and postoperative infections in patients undergoing primary coronary artery bypass surgery (CABG) [abstract]. Infect Control Hosp Epidemiol 1997; 18(No. 5, Part 2):29(58).
112. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A. Glucose control lowers the risk of wound infection in diabetics after open heart operations. Ann Thorac Surg 1997;63(2):356-61.
113. Terranova A. The effects of diabetes mellitus on wound healing. Plast Surg Nurs 1991;11(1):20-5.
114. Ziv Y, Church JM, Fazio VW, King TM, Lavery IC. Effect of systemic steroids on ileal pouch-anal anastomosis in patients with ulcerative colitis. Dis Colon Rectum 1996;39(5):504-8.

115. Pons VG, Denlinger SL, Guglielmo BJ, Octavio J, Flaherty J, Derish PA, et al. Ceftizoxime versus vancomycin and gentamicin in neurosurgical prophylaxis: a randomized, prospective, blinded clinical study. Neurosurgery 1993;33(3):416-22; discussion 422-3.
116. Brown IW Jr, Moor GF, Hummel BW, Marshall WG Jr, Collins JP. Toward further reducing wound infections in cardiac operations. Ann Thorac Surg 1996;62(6):1783-9.
117. Christou NV, Nohr CW, Meakins JL. Assessing operative site infection in surgical patients. Arch Surg 1987;122:165-9.
118. Hu SS, Fontaine F, Kelly B, Bradford DS. Nutritional depletion in staged spinal reconstructive surgery. The effect of total parenteral nutrition. Spine 1998;23:1401-5.
119. Schackert HK, Betzler M, Zimmermann GF, Decker R, Geelhaar H, Edler L, et al. The predictive role of delayed cutaneous hypersensitivity testing in postoperative complications. Surg Gynecol Obstet 1986;162:563-8.
120. Katelaris PH, Bennett GB, Smith RC. Prediction of postoperative complications by clinical and nutritional assessment. Aust N Z J Surg 1986;56:743-7.
121. Leite JF, Antunes CF, Monteiro JC, Pereira BT. Value of nutritional parameters in the prediction of postoperative complications in elective gastrointestinal surgery. Br J Surg 1987;74:426-9.
122. Mullen JL, Gertner MH, Buzby GP, Goodhart GL, Rosato EF. Implications of malnutrition in the surgical patient. Arch Surg 1979;114:121-5.
123. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. Am J Surg 1980;139:160-7.
124. Ellis LM, Copeland EM 3rd, Souba WW. Perioperative nutritional support. Surg Clin North Am 1991;71:493-507.
125. Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM. Identifying patients at high risk of surgical wound infection. A simple multivariate index of patient susceptibility and wound contamination. Am J Epidemiol 1985;121:206-15.
126. Culver DH, Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG, et al. Surgical wound infection rates by wound class, operative procedure, and patient risk index. National Nosocomial Infections Surveillance System. Am J Med 1991;91(Suppl 3B):152S-7S.
127. Windsor JA, Hill GL. Weight loss with physiologic impairment. A basic indicator of surgical risk. Ann Surg 1988;207:290-6.
128. Campos AC, Meguid MM. A critical appraisal of the usefulness of perioperative nutritional support. Am J Clin Nutr 1992;55:117-30.
129. McPhee IB, Williams RP, Swanson CE. Factors influencing wound healing after surgery for metastatic disease of the spine. Spine 1998;23:726-33; discussion 732-3.
130. Mullen JL, Buzby GP, Matthews DC, Smale BF, Rosato EF. Reduction of operative morbidity and mortality by combined preoperative and postoperative nutritional support. Ann Surg 1980;192:604-13.
131. Windsor JA, Hill GL. Protein depletion and surgical risk. Aust N Z J Surg 1988;58:711-5.
132. Ulicny KS Jr, Hiratzka LF, Williams RB, Grunkemeier GL, Flege JB, Jr., Wright CB, et al. Sternotomy infection: poor prediction by acute phase response and delayed hypersensitivity. Ann Thorac Surg 1990;50:949-58.
133. Shukla HS, Rao RR, Banu N, Gupta RM, Yadav RC. Enteral hyperalimentation in malnourished surgical patients. Indian J Med Res 1984;80:339-46.
134. Moore EE, Jones TN. Benefits of immediate jejunostomy feeding after major abdominal trauma—a prospective, randomized study. J Trauma 1986;26:874-81.
135. Daly JM, Lieberman MD, Goldfine J, Shou J, Weintraub F, Rosato EF, et al. Enteral nutrition with supplemental arginine, RNA, and omega-3 fatty acids in patients after operation: immunologic, metabolic, and clinical outcome. Surgery 1992;112:56-67.
136. Daly JM, Weintraub FN, Shou J, Rosato EF, Lucia M. Enteral nutrition during multimodality therapy in upper gastrointestinal cancer patients. Ann Surg 1995;221:327-38.
137. Moore FA, Feliciano DV, Andrassy RJ, McArdle AH, Booth FV, Morgenstein-Wagner TB, et al. Early enteral feeding, compared with parenteral, reduces postoperative septic complications. The results of a meta-analysis. Ann Surg 1992;216:172-83.
138. Starker PM, Lasala PA, Askanazi J, Gump FE, Forse RA, Kinney JM. The response to TPN: a form of nutritional assessment. Ann Surg 1983;198:720-4.
139. Muller JM, Brenner U, Dienst C, Pichlmaier H. Preoperative parenteral feeding in patients with gastrointestinal carcinoma. Lancet 1982;1:68-71.
140. Holter AR, Fischer JE. The effects of perioperative hyperalimentation on complications in patients with carcinoma and weight loss. J Surg Res 1977;23:31-4.
141. Thompson BR, Julian TB, Stremple JF. Perioperative total parenteral nutrition in patients with gastrointestinal cancer. J Surg Res 1981;30:497-500.
142. Brennan MF, Pisters PW, Posner M, Quesada O, Shike M. A prospective randomized trial of total parenteral nutrition after major pancreatic resection for malignancy. Ann Surg 1994;220:436-41; discussion 441-4.
143. The Veterans Affairs Total Parental Nutrition Cooperative Study Group. Perioperative total parenteral nutrition in surgical patients. N Engl J Med 1991;325:525-32.
144. Starker PM, LaSala PA, Askanazi J, Todd G, Hensle TW, Kinney JM. The influence of preoperative total parenteral nutrition upon morbidity and mortality. Surg Gynecol Obstet 1986;162:569-74.
145. Senkal M, Mumme A, Eickhoff U, Geier B, Spath G, Wulfert D, et al. Early postoperative enteral immunonutrition: clinical outcome and cost-comparison analysis in surgical patients. Crit Care Med 1997;25:1489-96.
146. Heatley RV, Williams RH, Lewis MH. Pre-operative intravenous feeding—a controlled trial. Postgrad Med J 1979;55:541-5.
147. Muller JM, Keller HW, Brenner U, Walter M, Holzmuller W. Indications and effects of preoperative parenteral nutrition. World J Surg 1986;10:53-63.
148. Daly JM, Massar E, Giacco G, Frazier OH, Mountain CF, Dudrick SJ, et al. Parenteral nutrition in esophageal cancer patients. Ann Surg 1982;196:203-8.
149. Klein JD, Hey LA, Yu CS, Klein BB, Coufal FJ, Young EP, et al. Perioperative nutrition and postoperative complications in patients undergoing spinal surgery. Spine 1996;21:2676-82.
150. Garibaldi RA, Cushing D, Lerer T. Risk factors for postoperative infection. Am J Med 1991;91(Suppl 3B):158S-63S.
151. Lee JT. Operative complications and quality improvement. Am J Surg 1996;171:545-7.
152. Kluytmans JA, Mouton JW, VandenBergh MF, Manders MJ, Maat AP, et al. Reduction of surgical-site infections in cardiothoracic surgery by elimination of nasal carriage of *Staphylococcus aureus*. Infect Control Hosp Epidemiol 1996;17:780-5.
153. Boyce JM. Preventing staphylococcal infections by eradicating nasal carriage of *Staphylococcus aureus*: proceeding with caution. Infect Control Hosp Epidemiol 1996;17:775-9.
154. Blajchman MA. Allogeneic blood transfusions, immunomodulation, and postoperative bacterial infection: do we have the answers yet? Transfusion 1997;37:121-5.
155. Garibaldi RA. Prevention of intraoperative wound contamination with chlorhexidine shower and scrub. J Hosp Infect 1988;11(Suppl B):5-9.

156. Paulson DS. Efficacy evaluation of a 4% chlorhexidine gluconate as a full-body shower wash. Am J Infect Control 1993;21(4):205-9.
157. Hayek LJ, Emerson JM, Gardner AM. A placebo-controlled trial of the effect of two preoperative baths or showers with chlorhexidine detergent on postoperative wound infection rates. J Hosp Infect 1987;10:165-72.
158. Kaiser AB, Kernodle DS, Barg NL, Petracek MR. Influence of preoperative showers on staphylococcal skin colonization: a comparative trial of antiseptic skin cleansers. Ann Thorac Surg 1988;45:35-8.
159. Rotter ML, Larsen SO, Cooke EM, Dankert J, Daschner F, Greco D, et al. A comparison of the effects of preoperative whole-body bathing with detergent alone and with detergent containing chlorhexidine gluconate on the frequency of wound infections after clean surgery. The European Working Party on Control of Hospital Infections. J Hosp Infect 1988;11:310-20.
160. Leigh DA, Stronge JL, Marriner J, Sedgwick J. Total body bathing with 'Hibiscrub' (chlorhexidine) in surgical patients: a controlled trial. J Hosp Infect 1983;4:229-35.
161. Ayliffe GA, Noy MF, Babb JR, Davies JG, Jackson J. A comparison of pre-operative bathing with chlorhexidine-detergent and non-medicated soap in the prevention of wound infection. J Hosp Infect 1983;4:237-44.
162. Lynch W, Davey PG, Malek M, Byrne DJ, Napier A. Cost-effectiveness analysis of the use of chlorhexidine detergent in preoperative whole-body disinfection in wound infection prophylaxis. J Hosp Infect 1992;21:179-91.
163. Brady LM, Thomson M, Palmer MA, Harkness JL. Successful control of endemic MRSA in a cardiothoracic surgical unit. Med J Aust 1990;152:240-5.
164. Tuffnell DJ, Croton RS, Hemingway DM, Hartley MN, Wake PN, Garvey RJ. Methicillin-resistant Staphylococcus aureus; the role of antisepsis in the control of an outbreak. J Hosp Infect 1987;10:255-9.
165. Bartzokas CA, Paton JH, Gibson MF, Graham F, McLoughlin GA, Croton RS. Control and eradication of methicillin-resistant Staphylococcus aureus on a surgical unit. N Engl J Med 1984;311:1422-5.
166. Seropian R, Reynolds BM. Wound infections after preoperative depilatory versus razor preparation. Am J Surg 1971;121:251-4.
167. Hamilton HW, Hamilton KR, Lone FJ. Preoperative hair removal. Can J Surg 1977;20:269-71, 274-5.
168. Olson MM, MacCallum J, McQuarrie DG. Preoperative hair removal with clippers does not increase infection rate in clean surgical wounds. Surg Gynecol Obstet 1986;162:181-2.
169. Mehta G, Prakash B, Karmoker S. Computer assisted analysis of wound infection in neurosurgery. J Hosp Infect 1988;11:244-52.
170. Alexander JW, Fischer JE, Boyajian M, Palmquist J, Morris MJ. The influence of hair-removal methods on wound infections. Arch Surg 1983;118(3):347-52.
171. Masterson TM, Rodeheaver GT, Morgan RF, Edlich RF. Bacteriologic evaluation of electric clippers for surgical hair removal. Am J Surg 1984;148:301-2.
172. Sellick JA Jr., Stelmach M, Mylotte JM. Surveillance of surgical wound infections following open heart surgery. Infect Control Hosp Epidemiol 1991;12(10):591-6.
173. Ko W, Lazenby WD, Zelano JA, Isom W, Krieger KH. Effects of shaving methods and intraoperative irrigation on suppurative mediastinitis after bypass operations. Ann Thorac Surg 1992;53:301-5.
174. Moro ML, Carrieri MP, Tozzi AE, Lana S, Greco D. Risk factors for surgical wound infections in clean surgery: a multicenter study. Italian PRINOS Study Group. Ann Ital Chir 1996;67:13-9.
175. Winston KR. Hair and neurosurgery. Neurosurgery 1992;31(2):320-9.
176. Larson E. Guideline for use of topical antimicrobial agents. Am J Infect Control 1988;16:253-66.
177. Hardin WD, Nichols RL. Handwashing and patient skin preparation. In: Malangoni MA, ed. Critical Issues in Operating Room Management. Philadelphia: Lippincott-Raven; 1997. p. 133-49.
178. Ritter MA, French ML, Eitzen HE, Gioe TJ. The antimicrobial effectiveness of operative-site preparative agents: a microbiological and clinical study. J Bone Joint Surg Am 1980;62(5):826-8.
179. Mayhall CG. Surgical infections including burns. In: Wenzel RP, ed. Prevention and Control of Nosocomial Infections. 2nd ed. Baltimore: Williams & Wilkins; 1993. p. 614-64.
180. Committee on Control of Surgical Infections of the Committee on Pre- and Postoperative care, American College of Surgeons. Manual on Control of Infection in Surgical Patients. Philadelphia: J.B. Lippincott Co; 1984.
181. Hardin WD, Nichols RL. Aseptic technique in the operating room. In: Fry DE, ed. Surgical Infections. Boston: Little, Brown and Co; 1995. p. 109-18.
182. Lowbury EJ, Lilly HA. Use of 4 percent chlorhexidine detergent solution (Hibiscrub) and other methods of skin disinfection. Br Med J 1973;1:510-5.
183. Aly R, Maibach HI. Comparative antibacterial efficacy of a 2-minute surgical scrub with chlorhexidine gluconate, povidone-iodine, and chloroxylenol sponge-brushes. Am J Infect Control 1988;16:173-7.
184. Peterson AF, Rosenberg A, Alatary SD. Comparative evaluation of surgical scrub preparations. Surg Gynecol Obstet 1978;146:63-5.
185. Brown TR, Ehrlich CE, Stehman FB, Golichowski AM, Madura JA, Eitzen HE. A clinical evaluation of chlorhexidine gluconate spray as compared with iodophor scrub for preoperative skin preparation. Surg Gynecol Obstet 1984;158:363-6.
186. Lowbury EJ, Lilly HA. The effect of blood on disinfection of surgeons' hands. Br J Surg 1974;61:19-21.
187. Association of Operating Room Nurses. Recommended practices for skin preparation of patients. AORN J 1996;64(5):813-6.
188. Kutarski PW, Grundy HC. To dry or not to dry? An assessment of the possible degradation in efficiency of preoperative skin preparation caused by wiping skin dry. Ann R Coll Surg Engl 1993;75(3):181-5.
189. Gauthier DK, O'Fallon PT, Coppage D. Clean vs sterile surgical skin preparation kits. Cost, safety, effectiveness. AORN J 1993;58(3):486-95.
190. Hagen KS, Treston-Aurand J. A comparison of two skin preps used in cardiac surgical procedures. AORN J 1995;62(3):393-402.
191. Shirahatti RG, Joshi RM, Vishwanath YK, Shinkre N, Rao S, Sankpal JS, et al. Effect of pre-operative skin preparation on post-operative wound infection. J Postgrad Med 1993;39(3):134-6.
192. Larson EL, Butz AM, Gullette DL, Laughon BA. Alcohol for surgical scrubbing? Infect Control Hosp Epidemiol 1990;11(3):139-43.
193. Faoagali J, Fong J, George N, Mahoney P, O'Rouke V. Comparison of the immediate, residual, and cumulative antibacterial effects of Novaderm R*, Novascrub R*, Betadine Surgical Scrub, Hibiclens, and liquid soap. Am J Infect Control 1995;23(6):337-43.
194. Larson EL. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995;23:251-69.
195. Rubio PA. Septisol antiseptic foam: a sensible alternative to the conventional surgical scrub. Int Surg 1987;72(4):243-6.
196. Lowbury EJ, Lilly HA, Ayliffe GA. Preoperative disinfection of surgeons' hands: use of alcoholic solutions and effects of gloves on skin flora. Br Med J 1974;4:369-72.
197. Rotter ML. Hygienic hand disinfection. Infect Control 1984;5:18-22.
198. Ayliffe GA. Surgical scrub and skin disinfection. Infect Control 1984;5:23-7.
199. Lilly HA, Lowbury EJ, Wilkins MD, Zaggy A. Delayed antimicro-

bial effects of skin disinfection by alcohol. J Hyg (Lond) 1979;82:497-500.
200. Nichols RL, Smith JW, Garcia RY, Waterman RS, Holmes JW. Current practices of preoperative bowel preparation among North American colorectal surgeons. Clin Infect Dis 1997;24:609-19.
201. Wade JJ, Casewell MW. The evaluation of residual antimicrobial activity on hands and its clinical relevance. J Hosp Infect 1991;18(Suppl B):23-8.
202. Babb JR, Davies JG, Ayliffe GA. A test procedure for evaluating surgical hand disinfection. J Hosp Infect 1991;18(Suppl B):41-9.
203. Holloway PM, Platt JH, Reybrouck G, Lilly HA, Mehtar S, Drabu Y. A multi-centre evaluation of two chlorhexidine-containing formulations for surgical hand disinfection. J Hosp Infect 1990;16:151-9.
204. Kobayashi H. Evaluation of surgical scrubbing. J Hosp Infect 1991;18(Suppl B):29-34.
205. Nicoletti G, Boghossian V, Borland R. Hygienic hand disinfection: a comparative study with chlorhexidine detergents and soap. J Hosp Infect 1990;15:323-37.
206. Rotter ML, Koller W. Surgical hand disinfection: effect of sequential use of two chlorhexidine preparations. J Hosp Infect 1990;16:161-6.
207. O'Shaughnessy M, O'Malley VP, Corbett G, Given HF. Optimum duration of surgical scrub-time. Br J Surg 1991;78(6):685-6.
208. Hingst V, Juditzki I, Heeg P, Sonntag HG. Evaluation of the efficacy of surgical hand disinfection following a reduced application time of 3 instead of 5 min. J Hosp Infect 1992;20(2):79-86.
209. Wheelock SM, Lookinland S. Effect of surgical hand scrub time on subsequent bacterial growth. AORN J 1997;65:1087-92, 1094-8.
210. Deshmukh N, Kramer JW, Kjellberg SI. A comparison of 5-minute povidone-iodine scrub and 1-minute povidone-iodine scrub followed by alcohol foam. Mil Med 1998;163:145-7.
211. Masterson BJ. Cleansing the surgeon's hands. Scientific American Surgeon 1996;2:3-9.
212. Association of Operating Room Nurses. Standards, Recommended Practices, Guidelines. Denver: Association of Operating Room Nurses; 1999.
213. Pottinger J, Burns S, Manske C. Bacterial carriage by artificial versus natural nails. Am J Infect Control 1989;17:340-4.
214. Passaro DJ, Waring L, Armstrong R, Bolding F, Bouvier B, Rosenberg J, et al. Postoperative *Serratia marcescens* wound infections traced to an out-of-hospital source. J Infect Dis 1997; 175(4):992-5.
215. Baumgardner CA, Maragos CS, Walz J, Larson E. Effects of nail polish on microbial growth of fingernails. Dispelling sacred cows. AORN J 1993;58:84-8.
216. Jacobson G, Thiele JE, McCune JH, Farrell LD. Handwashing: ring-wearing and number of microorganisms. Nurs Res 1985;34:186-8.
217. Hoffman PN, Cooke EM, McCarville MR, Emmerson AM. Micro-organisms isolated from skin under wedding rings worn by hospital staff. Br Med J (Clin Res Ed) 1985;290:206-7.
218. Richet HM, Chidiac C, Prat A, Pol A, David M, Maccario M, et al. Analysis of risk factors for surgical wound infections following vascular surgery. Am J Med 1991;91(Suppl 3B):170S-172S.
219. Centers for Disease Control. Epidemic keratoconjunctivitis in an ophthalmology clinic—California. MMWR 1990;39:598-601.
220. Ford E, Nelson KE, Warren D. Epidemiology of epidemic keratoconjunctivitis. Epidemiol Rev 1987;9:244-61.
221. Birenbaum E, Linder N, Varsano N, Azar R, Kuint J, Spierer A, et al. Adenovirus type 8 conjunctivitis outbreak in a neonatal intensive care unit. Arch Dis Child 1993;68(5 Spec No):610-1.
222. Warren D, Nelson KE, Farrar JA, Hurwitz E, Hierholzer J, Ford E, et al. A large outbreak of epidemic keratoconjunctivitis: problems in controlling nosocomial spread. J Infect Dis 1989;160:938-43.
223. Jernigan JA, Lowry BS, Hayden FG, Kyger SA, Conway BP, Groschel DH, et al. Adenovirus type 8 epidemic keratoconjunctivitis in an eye clinic: risk factors and control. J Infect Dis 1993;167:1307-13.
224. Boyce JM. Should we vigorously try to contain and control methicillin-resistant *Staphylococcus aureus*? Infect Control Hosp Epidemiol 1991;12:46-54.
225. Boyce JM, Opal SM, Potter-Bynoe G, Medeiros AA. Spread of methicillin-resistant *Staphylococcus aureus* in a hospital after exposure to a health care worker with chronic sinusitis. Clin Infect Dis 1993;17:496-504.
226. Sheretz RJ, Reagan DR, Hampton KD, Robertson KL, Streed SA, Hoen HM, et al. A cloud adult: the *Staphylococcus aureus*-virus interaction revisited. Ann Intern Med 1996;124:539-47.
227. Belani A, Sherertz RJ, Sullivan ML, Russell BA, Reumen PD. Outbreak of staphylococcal infection in two hospital nurseries traced to a single nasal carrier. Infect Control 1986;7:487-90.
228. Kreiswirth BN, Kravitz GR, Schlievert PM, Novick RP. Nosocomial transmission of a strain of *Staphylococcus aureus* causing toxic shock syndrome. Ann Intern Med 1986;105:704-7.
229. Weber DJ, Rutala WA, Denny FW Jr. Management of healthcare workers with pharyngitis or suspected streptococcal infections. Infect Control Hosp Epidemiol 1996;17:753-61.
230. Viglionese A, Nottebart VF, Bodman HA, Platt R. Recurrent group A streptococcal carriage in a health care worker associated with widely separated nosocomial outbreaks. Am J Med 1991;91(3B):329S-33S.
231. Paul SM, Genese C, Spitalny K. Postoperative group A beta-hemolytic *streptococcus* outbreak with the pathogen traced to a member of a healthcare worker's household. Infect Control Hosp Epidemiol 1990;11:643-6.
232. Ridgway EJ, Allen KD. Clustering of group A streptococcal infections on a burns unit: important lessons in outbreak management. J Hosp Infect 1993;25:173-82.
233. Berkelman RL, Martin D, Graham DR, Mowry J, Freisem R, Weber JA, et al. Streptococcal wound infection caused by a vaginal carrier. JAMA 1982;247:2680-2.
234. Schaffner W, Lefkowitz LB Jr., Goodman JS, Koenig MG. Hospital outbreak of infections with group A streptococci traced to an asymptomatic anal carrier. N Engl J Med 1969;280:1224-5.
235. Richman DD, Breton SJ, Goldman DA. Scarlet fever and group A streptococcal surgical wound infection traced to an anal carrier. J Pediatr 1977;90:387-90.
236. Stromberg A, Schwan A, Cars O. Throat carrier rates of beta-hemolytic streptococci among healthy adults and children. Scand J Infect Dis 1988;20:411-7.
237. Stamm WE, Feeley JC, Facklam RR. Wound infection due to group A *streptococcus* traced to a vaginal carrier. J Infect Dis 1978;138:287-92.
238. Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchman SD, et al. Guideline for infection control in healthcare personnel, 1998. Hospital Infection Control Practices Advisory Committee. Am J Infect Control 1998;26:289-354.
239. Nichols RL, Holmes JW. Prophylaxis in bowel surgery. Curr Clin Top Infect Dis 1995;15:76-96.
240. Nichols RL, Smith JW, Muzik AC, Love EJ, McSwain NE, Timberlake G, et al. Preventive antibiotic usage in traumatic thoracic injuries requiring closed tube thoracostomy. Chest 1994;106(5):1493-8.
241. Bullock R, van Dellen JR, Ketelbey W, Reinach SG. A double-blind placebocontrolled trial of perioperative prophylactic antibiotics for elective neurosurgery. J Neurosurg 1988;69(5):687-91.
242. Page CP, Bohnen JM, Fletcher JR, McManus AT, Solomkin JS, Wittmann DH. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. Arch Surg 1993;128(1):79-88.

243. McQueen M, Littlejohn A, Hughes SP. A comparison of systemic cefuroxime and cefuroxime loaded bone cement in the prevention of early infection after total joint replacement. Int Orthop 1987;11:241-3.
244. Henley MB, Jones RE, Wyatt RWB, Hofmann A, Cohen RL. Prophylaxis with cefamandole nafate in elective orthopedic surgery. Clin Orthop 1986;209:249-54.
245. Buckley R, Hughes GN, Snodgrass T, Huchcroft SA. Perioperative cefazolin prophylaxis in hip fracture surgery. Can J Surg 1990;33:122-7.
246. Boyd RJ, Burke JF, Colton T. A double-blind clinical trial of prophylactic antibiotic in hip fractures. J Bone Joint Surg [Am] 1973;55A:1251-8.
247. Bernard A, Pillet M, Goudet P, Viard H. Antibiotic prophylaxis in pulmonary surgery. A prospective randomized double-blind trial of flash cefuroxime versus forty-eight-hour cefuroxime. J Thorac Cardiovasc Surg 1994;107(3):896-900.
248. Platt R, Zucker JR, Zaleznik DF, Hopkins CC, Dellinger EP, Karchmer AW, et al. Perioperative antibiotic prophylaxis and wound infection following breast surgery. J Antimicrob Chemother 1993;31(Suppl B):43-8.
249. Rimoldi RL, Haye W. The use of antibiotics for wound prophylaxis in spinal surgery. Orthop Clin North Am 1996;27(1):47-52.
250. Bennion RS, Hiatt JR, Williams RA, Wilson SE. A randomized, prospective study of perioperative antimicrobial prophylaxis for vascular access surgery. J Cardiovasc Surg (Torino) 1985;26:270-4.
251. Kaiser AB, Petracek MR, Lea JW 4th, Kernodle DS, Roach AC, Alford WC Jr, et al. Efficacy of cefazolin, cefamandole, and gentamicin as prophylactic agents in cardiac surgery. Results of a prospective, randomized, double-blind trial in 1030 patients. Ann Surg 1987;206(6):791-7.
252. Miedzinski LJ, Callaghan JC, Fanning EA, Gelfand ET, Goldsand G, Modry D, et al. Antimicrobial prophylaxis for open heart operations. Ann Thorac Surg 1990;50:800-7.
253. Doebbeling BN, Pfaller MA, Kuhns KR, Massanari RM, Behrendt DM, Wenzel RP. Cardiovascular surgery prophylaxis. A randomized, controlled comparison of cefazolin and cefuroxime. J Thorac Cardiovasc Surg 1990;99:981-9.
254. Madsen MS, Neumann L, Andersen JA. Penicillin prophylaxis in complicated wounds of hands and feet: a randomized , double-blind trial. Injury 1996;27(4):275-8.
255. Burnett JW, Gustilo RB, Williams DN, Kind AC. Prophylactic antibiotics in hip fractures. A double-bind, prospective study. J Bone Joint Surg [Am]1980;62(3):457-62.
256. Nichols RL, Webb WR, Jones JW, Smith JW, LoCicero J 3rd. Efficacy of antibiotic prophylaxis in high risk gastroduodenal operations. Am J Surg 1982;143:94-8.
257. Lewis RT, Goodall RG, Marien B, Park M, Lloyd-Smith W, Wiegand FM. Efficacy and distribution of single-dose preoperative antibiotic prophylaxis in high-risk gastroduodenal surgery. Can J Surg 1991;34:117-22.
258. Young RF, Lawner PM. Perioperative antibiotic prophylaxis for prevention of postoperative neurosurgical infections. A randomized clinical trial. J Neurosurg 1987;66:701-5.
259. Djindjian M, Lepresle E, Homs JB. Antibiotic prophylaxis during prolonged clean neurosurgery. Results of a randomized double-blind study using oxacillin. J Neurosurg 1990;73:383-6.
260. Targarona EM, Garau J, Munoz-Ramos C, Roset F, Lite J, Matas E, et al. Single-dose antibiotic prophylaxis in patients at high risk for infection in biliary surgery: a prospective and randomized study comparing cefonicid with mezlocillin. Surgery 1990;107:327-34.
261. van Ek B, Dijkmans BA, van Dulken H, van Furth R. Antibiotic prophylaxis in craniotomy: a prospective double-blind placebo-controlled study. Scand J Infect Dis 1988;20:633-9.
262. Krige JE, Isaacs S, Stapleton GN, McNally J. Prospective, randomized study comparing amoxycillin-clavulanic acid and cefamandole for the prevention of wound infection in high-risk patients undergoing elective biliary surgery. J Hosp Infect 1992;22 (Suppl A):33-41.
263. Browder W, Smith JW, Vivoda LM, Nicholas RL. Nonperforative appendicitis: a continuing surgical dilemma. J Infect Dis 1989;159(6):1088-94.
264. Platt R. Guidelines for perioperative antibiotic prophylaxis. In: Abrutyn E, Goldmann DA, Scheckler WE, eds. Saunders infection control reference service. Philadelphia: W.B. Saunders Co; 1997. p. 229-34.
265. Sanderson PJ. Antimicrobial prophylaxis in surgery: microbiological factors. J Antimicrob Chemother 1993;31(Suppl B):1-9.
266. Anonymous. Antimicrobial prophylaxis in surgery. Med Lett Drugs Ther 1997;39(1012):97-102.
267. Scher KS. Studies on the duration of antibiotic administration for surgical prophylaxis. Am Surg 1997;63:59-62.
268. Nichols RL. Antibiotic prophylaxis in surgery. J Chemother 1989;1(3):170-8.
269. Ehrenkranz NJ. Antimicrobial prophylaxis in surgery: mechanisms, misconceptions, and mischief. Infect Control Hosp Epidemiol 1993;14(2):99-106.
270. Berkeley AS, Freedman KS, Ledger WJ, Orr JW, Benigno BB, Gordon SF, et al. Comparison of cefotetan and cefoxitin prophylaxis for abdominal and vaginal hysterectomy. Am J Obstet Gynecol 1988;158:706-9.
271. Ehrenkranz NJ, Blackwelder WC, Pfaff SJ, Poppe D, Yerg DE, Kaslow RA. Infections complicating low-risk cesarean sections in community hospitals: efficacy of antimicrobial prophylaxis. Am J Obstet Gynecol 1990;162(2):337-43.
272. Soper DE. Infections following cesarean section. Curr Opin Obstet Gynecol 1993;5(4):517-20.
273. Enkin M, Enkin E, Chalmers I, Hemminki E. Prophylactic antibiotics in association with caesarean section. In: Chalmers I, Enkin M, Keirse MJ, eds. Effective care in pregnancy and childbirth. London: Oxford University; 1989. p. 1246-69.
274. Allen JL, Rampon JF, Wheeless CR. Use of a prophylactic antibiotic in elective major gynecologic operations. Obstet Gynecol 1972;39:218-24.
275. The Multicenter Study Group. Single dose prophylaxis in patients undergoing vaginal hysterectomy: cefamandole versus cefotaxime. Am J Obstet Gynecol 1989;160:1198-201.
276. Roy S, Wilkins J, Galaif E, Azen C. Comparative efficacy and safety of cefmetazole or cefoxitin in the prevention of postoperative infection following vaginal and abdominal hysterectomy. J Antimicrob Chemother 1989;23(Suppl D):109-17.
277. Friese S, Willems FT, Loriaux SM, Meewis JM. Prophylaxis in gynaecological surgery: a prospective randomized comparison between single dose prophylaxis with amoxycillin/clavulanate and the combination of cefuroxime and metronidazole. J Antimicrob Chemother 1989;24(Suppl B):213-6.
278. Senior CC, Steigrad SJ. Are preoperative antibiotics helpful in abdominal hysterectomy? Am J Obstet Gynecol 1986;154:1004-8.
279. Hemsell DL, Martin JN Jr, Pastorek JG 2d, Nobles BJ, Hemsell PG, Helman N, et al. Single dose antimicrobial prophylaxis at abdominal hysterectomy. Cefamandole vs. cefotaxime. J Reprod Med 1988;33:939-44.
280. Hemsell DL, Hemsell PG, Heard ML, Nobles BJ. Preoperative cefoxitin prophylaxis for elective abdominal hysterectomy. Am J Obstet Gynecol 1985;153:225-6.
281. DiPiro JT, Cheung RP, Bowden TA Jr, Mansberger JA. Single dose systemic antibiotic prophylaxis of surgical wound infections. Am J Surg 1986;152:552-9.

282. Trilla A, Mensa J. Perioperative antibiotic prophylaxis. In: Wenzel RP, ed. Prevention and control of nosocomial infections. 2nd ed. Baltimore: Williams & Wilkins; 1993. p. 665-82.
283. Ehrenkranz NJ, Meakins JL. Surgical infections. In: Bennett JV, Brachman PS, eds. Hospital infections. 3rd ed. Boston: Little, Brown and Co; 1992. p. 685-710.
284. Nichols RL. Surgical antibiotic prophylaxis. Med Clin North Am 1995;79(3):509-22.
285. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 1992;326(5):281-6.
286. McDonald M, Grabsch E, Marshall C, Forbes A. Single- versus multiple-dose antimicrobial prophylaxis for major surgery: a systematic review. Aust N Z J Surg 1998;68:388-96.
287. Clarke JS, Condon RE, Bartlett JG, Gorbach SL, Nichols RL, Ochi S. Preoperative oral antibiotics reduce septic complications of colon operations: results of prospective, randomized, double-blind clinical study. Ann Surg 1977;186:251-9.
288. Condon RE, Bartlett JG, Greenlee H, Schulte WJ, Ochi S, Abbe R, et al. Efficacy of oral and systemic antibiotic prophylaxis in colorectal operations. Arch Surg 1983;118:496-502.
289. Bartlett JG, Condon RE, Gorbach SL, Clarke JS, Nichols RL, Ochi S. Veterans Administration Cooperative Study on bowel preparation for elective colorectal operation: impact of oral antibiotic regimen on colonic flora, wound irrigation cultures and bacteriology of septic complications. Ann Surg 1978; 188:249-54.
290. Da Costa A, Kirkorian G, Cucherat M, Delahaye F, Chevalier P, Cerisier A, et al. Antibiotic prophylaxis for permanent pacemaker implantation: a meta-analysis. Circulation 1998;97:1796-801.
291. Bumpous JM, Johnson JT. The infected wound and its management. Otolaryngol Clin North Am 1995;28(5):987-1001.
292. Hospital Infection Control Practices Advisory Committee. Recommendations for preventing the spread of vancomycin resistance. Infect Control Hosp Epidemiol 1995;16(2):105-13.
293. Forse RA, Karam B, MacLean LD, Christou NV. Antibiotic prophylaxis for surgery in morbidly obese patients. Surgery 1989;106:750-7.
294. Polk HC, Wilson MA. Systemic antibiotic prophylaxis in surgery. In: Fry DE, ed. Surgical infections. Boston: Little, Brown and Co; 1995. p. 127-33.
295. Ayliffe GA. Role of the environment of the operating suite in surgical wound infection. Rev Infect Dis 1991;13(Suppl 10):S800-4
296. Gryska PF, O'Dea AE. Postoperative streptococcal wound infection. The anatomy of an epidemic. JAMA 1970;213:1189-91.
297. McIntyre DM. An epidemic of *Streptococcus pyogenes* puerperal and postoperative sepsis with an unusual carrier site—the anus. Am J Obstet Gynecol 1968;101:308-14.
298. Lidwell OM. Clean air at operation and subsequent sepsis in the joint. Clin Orthop 1986;211:91-102.
299. American Institute of Architects. Guidelines for design and construction of hospital and health care facilities. Washington: American Instituite of Architects Press; 1996.
300. Nichols RL. The operating room. In: Bennett JV, Brachman PS, eds. Hospital infections. 3rd ed. Boston: Little, Brown and Co; 1992. p. 461-73.
301. Laufman H. The operating room. In: Bennett JV, Brachman PS, eds. Hospital Infections. 2nd ed. Boston: Little, Brown and Co; 1986. p. 315-23.
302. Sessler DI, McGuire J, Hynson J, Moayeri A, Heier T. Thermoregulatory vasoconstriction during isoflurane anesthesia minimally decreases cutaneous heat loss. Anesthesiology 1992;76:670-5.
303. Hambraeus A. Aerobiology in the operating room—a review. J Hosp Infect 1988;11(Suppl A):68-76
304. Babb JR, Lynam P, Ayliffe GA. Risk of airborne transmission in an operating theatre containing four ultraclean air units. J Hosp Infect 1995;31(3):159-68.
305. Charnley J. Post-operative infection after total hip replacement with special reference to contamination in the operating room. Internal Publication 38, Centre for Hip Surgery, Wrightington Hospital, Wigan, Lancs., UK; 1972.
306. Friberg B. Ultraclean laminar airflow ORs. AORN J 1998;67:841-51.
307. Lidwell OM, Elson RA, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, et al. Ultraclean air and antibiotics for prevention of postoperative infection. A multicenter study of 8,052 joint replacemnet operations. Acta Orthop Scand 1987;58:4-13.
308. Nelson JP. The operating room environment and its influence on deep wound infection. J Bone Joint Surg 1976;1-11.
309. Whyte W. Infection control in hospital operating rooms. Cleanrooms 1993 Proceedings 1993;157-66.
310. Charnley J. A clean-air operating enclosure. Br J Surg 1964;51:202-5.
311. Lidwell OM, Lowbury EJ, Whyte W, Blowers R, Stanley SJ, Lowe D. Effect of ultraclean air in operating rooms on deep sepsis in the joint after total hip or knee replacement: a randomised study. Br Med J 1982;285:10-4.
312. Taylor GJ, Bannister GC, Leeming JP. Wound disinfection with ultraviolet radiation. J Hosp Infect 1995;30(2):85-93.
313. Bueno Cavanillas A, Rodriguez-Contreras R, Delgado Rodriguez M, Moreno Abril O, Gigosos R, Guillen Solvas J, et al. Preoperative stay as a risk factor for nosocomial infection. Eur J Epidemiol 1991;7(6):670-6.
314. Favero MS, Bond W. Sterilization, disinfection, and antisepsis in the hospital. In: Balows A, Hausler WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of clinical microbiology. 5th ed. Washington, DC: American Society of Microbiology; 1991. p. 183-200.
315. U.S. Department of Labor, Occupational Safety and Health Administration. Occupational exposure to bloodborne pathogens; final rule (29 CFR Part 1910.1030). Federal Register 1991;56: 64004-182.
316. Rudnick JR, Beck-Sague CM, Anderson RL, Schable B, Miller JM, Jarvis WR. Gram-negative bacteremia in open-heart-surgery patients traced to probable tap-water contamination of pressure-monitoring equipment. Infect Control Hosp Epidemiol 1996;17(5):281-5.
317. Centers for Disease Control. Postsurgical infections associated with nonsterile implantable devices. MMWR Morb Mortal Wkly Rep 1992;41(15):263.
318. Soto LE, Bobadilla M, Villalobos Y, Sifuentes J, Avelar J, Arrieta M, et al. Post-surgical nasal cellulitis outbreak due to *Mycobacterium chelonae*. J Hosp Infect 1991;19(2):99-106.
319. Favero MS, Manian FA. Is eliminating flash sterilization practical? Infect Control Hosp Epidemiol 1993;14(8):479-80.
320. American Society for Healthcare Central Service Personnel. Recommended practices for central service. Section one, continuous quality improvement. Chicago: American Hospital Association; 1993.
321. Association for the Advancement of Medical Instrumentation. Flash sterilization: steam sterilization of patient care items for immediate use (ANSI/AAMI ST37-1996). Arlington (VA): Association for the Advancement of Medical Instrumentation; 1996.
322. Rutala WA, Gergen MF, Weber DJ. Evaluation of a rapid readout biological indicator for flash sterilization with three biological indicators and three chemical indicators. Infect Control Hosp Epidemiol 1993;14(7):390-4.

323. Vesley D, Langholz AC, Rohlfing SR, Foltz WE. Fluorimetric detection of a *Bacillus stearothermophilus* spore-bound enzyme, alpha-D-glucosidase, for rapid indication of flash sterilization failure. Appl Environ Microbiol 1992;58:717-9.
324. Rutala WA, Jones SM, Weber DJ. Comparison of a rapid readout biological indicator for steam sterilization with four conventional biological indicators and five chemical indicators. Infect Control Hosp Epidemiol 1996;17:423-8.
325. Vesley D, Nellis MA, Allwood PB. Evaluation of a rapid readout biological indicator for 121 degrees C gravity and 132 degrees C vacuum-assisted steam sterilization cycles. Infect Control Hosp Epidemiol 1995;16:281-6.
326. Smith RF. What is the purpose of the scrub suit? [letter]. AORN J 1980;31(5):769
327. Dineen P. The role of impervious drapes and gowns preventing surgical infection. Clin Orthop 1973;96:210-2.
328. Ha'eri GB, Wiley AM. The efficacy of standard surgical face masks: an investigation using "tracer particles". Clin Orthop 1980;148:160-2.
329. Moylan JA, Fitzpatrick KT, Davenport KE. Reducing wound infections. Improved gown and drape barrier performance. Arch Surg 1987;122:152-7.
330. Moylan JA, Balish E, Chan J. Intraoperative bacterial transmission. Surg Forum 1974;25:29-30.
331. Copp G, Mailhot CB, Zalar M, Slezak L, Copp AJ. Covergowns and the control of operating room contamination. Nurs Res 1986;35:263-8.
332. Beck WC. The surgical mask: another 'sacred cow'? AORN J 1992;55:955-7.
333. Mitchell NJ, Hunt S. Surgical face masks in modern operating rooms—a costly and unnecessary ritual? J Hosp Infect 1991;18:239-42.
334. Tunevall TG, Jorbeck H. Influence of wearing masks on the density of airborne bacteria in the vicinity of the surgical wound. Eur J Surg 1992;158(5):263-6.
335. Tunevall TG. Postoperative wound infections and surgical face masks: a controlled study. World J Surg 1991;15:383-8.
336. Orr NW. Is a mask necessary in the operating theatre? Ann R Coll Surg Engl 1981;63(6):390-2.
337. Lee JT. Making surgical care better: hard work, small gains [editorial]. Infect Control Hosp Epidemiol 1997;18:6-8.
338. Jarvis WR, Bolyard EA, Bozzi CJ, Burwen DR, Dooley SW, Martin LS, et al. Respirators, recommendations, and regulations: the controversy surrounding protection of health care workers from tuberculosis. Ann Intern Med 1995;122:142-6.
339. Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health. Protect yourself against tuberculosis: a respiratory protection guide for health care workers (Publication No. 96-102). Cincinnati: Department of Health and Human Services (NIOSH); 1995.
340. Humphreys H, Marshall RJ, Ricketts VE, Russell AJ, Reeves DS. Theatre over-shoes do not reduce operating theatre floor bacterial counts. J Hosp Infect 1991;17:117-23.
341. Weightman NC, Banfield KR. Protective over-shoes are unnecessary in a day surgery unit. J Hosp Infect 1994;28:1-3.
342. Whyte W, Hambraeus A, Laurell G, Hoborn J. The relative importance of routes and sources of wound contamination during general surgery. I. Non-airborne. J Hosp Infect 1991;18(2):93-107.
343. Dodds RD, Guy PJ, Peacock AM, Duffy SR, Barker SG, Thomas MH. Surgical glove perforation. Br J Surg 1988;75(10):966-8.
344. Tokars JI, Culver DH, Mendelson MH, Sloan EP, Farber BF, Fligner DJ, et al. Skin and mucous membrane contacts with blood during surgical procedures: risk and prevention. Infect Control Hosp Epidemiol 1995;16:703-11.
345. Short LJ, Bell DM. Risk of occupational infection with blood-borne pathogens in operating and delivery room settings. Am J Infect Control 1993;21:343-50.
346. Garibaldi RA, Maglio S, Lerer T, Becker D, Lyons R. Comparison of nonwoven and woven gown and drape fabric to prevent intraoperative wound contamination and postoperative infection. Am J Surg 1986;152(5):505-9.
347. Muller W, Jiru P, Mach R, Polaschek F, Fasching W. The use of disposable draping materials in the operating room and its effect on the postoperative wound infection rate. Wein Klin Wochenschr 1989;101:837-42.
348. Smith JW, Nichols RL. Barrier efficiency of surgical gowns. Are we really protected from our patients' pathogens? Arch Surg 1991;126(6):756-63.
349. Artz CP, Conn JH, Howard HS. Protection of the surgical wound with a new plastic film. JAMA 1960;174(14):1865-8.
350. Chiu KY, Lau SK, Fung B, Ng KH, Chow SP. Plastic adhesive drapes and wound infection after hip fracture surgery. Aust N Z J Surg 1993;63(10):798-801.
351. American Society for Testing Materials. Standard Test Method for Resistance of Materials used in Protective Clothing to Penetration by Synthetic Blood. American Society for Testing Materials 1998;F1670-98.
352. American Society for Testing Materials. Standard Test Method for Resistance of Materials used in Protective Clothing to Penetration by Blood-borne Pathogens using Phi-X174 Bacteriophage Penetration as a Test System. American Society for Testing Materials 1997; F1671-976.
353. McCullough EA. Methods for determining the barrier efficacy of surgical gowns. Am J Infect Control 1993;21:368-74.
354. Lewis JA, Brown PL. Breaking the comfort barrier in impervious gowns. Surgical Services Management 1998;4(2):29-38.
355. Granzow JW, Smith JW, Nichols RL, Waterman RS, Muzik AC. Evaluation of the protective value of hospital gowns against blood strike-through and methicillin-resistant *Staphylococcus aureus* penetration. Am J Infect Control 1998;26:85-93.
356. Walter CW, Kundsin RB, Harding AL, Page LK. The infector on the surgical team. Clin Neurosurg 1966;14:361-79.
357. Payne RW. Severe outbreak of surgical sepsis due to *Staphylococcus aureus* of unusual type and origin. Br Med J 1967;4:17-20.
358. Centers for Disease Control. Hospital outbreak of streptococcal wound infection-Utah. MMWR Morb Mortal Wkly Rep 1976;25:141
359. Herwaldt LA, Pottinger J, Coffin SA. Nosocomial infections associated with anesthesia. In: Mayhall CG, ed. Hospital epidemiology and infection control. Baltimore: Williams & Wilkins; 1996. p. 655-75.
360. Bennett SN, McNeil MM, Bland LA, Arduino MJ, Villarino ME, Perrotta DM, et al. Postoperative infections traced to contamination of an intravenous anesthetic, propofol. N Engl J Med 1995;333:147-54.
361. Froggatt JW, Dwyer DM, Stephens MA. Hospital outbreak of hepatitis B in patients undergoing electroconvulsive therapy [abstract]. Program and Abstracts of the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago 1991;157:(347).
362. Centers for Disease Control. Postsurgical infections associated with an extrinsically contaminated intravenous anesthetic agent—California, Illinois, Maine, and Michigan, 1990. MMWR Morb Mortal Wkly Rep 1990;39:426-7,433.
363. Daily MJ, Dickey JB, Packo KH. Endogenous *Candida* endophthalmitis after intravenous anesthsia with propofol. Arch Ophthalmol 1991;109:1081-4.

364. Villarino ME, McNeill MM, Hall WN. Postsurgical infections associated with an extrinsically contaminated intravenous anesthetic agent [abstract]. Program and Abstracts of the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago 1991;156:(346).
365. American Association of Nurse Anesthetists. Infection control guide. Park Ridge (IL): American Association of Nurse Anesthetists; 1993.
366. American Society of Anesthesiologists. Recommendations for infection control for the practice of anesthesiology. Park Ridge (IL): American Society of Anesthesiologists; 1992.
367. Garner JS, Favero MS. CDC guideline for handwashing and hospital environmental control, 1985. Infect Control 1986;7:231-43.
368. Zacharias A, Habib RH. Delayed primary closure of deep sternal wound infections. Tex Heart Inst J 1996;23(3):211-6.
369. Smilanich RP, Bonnet I, Kirkpactrick JR. Contaminated wounds: the effect of initial management on outcome. Am Surg 1995;61(5):427-30.
370. Blomstedt GC. Infections in neurosurgery: a randomized comparison between silk and polyglycolic acid. Acta Neurochir (Wien) 1985;76:90-3.
371. Scher KS, Bernstein JM, Jones CW. Infectivity of vascular sutures. Am Surg 1985;51:577-9.
372. Durdey P, Bucknall TE. Assessment of sutures for use in colonic surgery: an experimental study. J R Soc Med 1984;77:472-7.
373. Chu CC, Williams DF. Effects of physical configuration and chemical structure of suture materials on bacterial adhesion. A possible link to wound infection. Am J Surg 1984;147:197-204.
374. Askew AR. A comparison of upper abdominal wound closure with monofilament nylon and polyglycolic acid. Aust N Z J Surg 1983;53:353-6.
375. Kapadia CR, Mann JB, McGeehan D, Jose Biglin JE, Waxman BP, Dudley HA. Behaviour of synthetic absorbable sutures with and without synergistic enteric infection. Eur Surg Res 1983;15:67-72.
376. Bucknall TE, Teare L, Ellis H. The choice of a suture to close abdominal incisions. Eur Surg Res 1983;15:59-66.
377. Bucknall TE. Factors influencing wound compications: a clinical and experimental study. Ann R Coll Surg Engl 1983;65:71-7.
378. Varma S, Lumb WV, Johnson LW, Ferguson HL. Further studies with polyglycolic acid (Dexon) and other sutures in infected experimental wounds. Am J Vet Res 1981;42:571-4.
379. Bucknall TE, Ellis H. Abdominal wound closure—a comparison of monofilament nylon and polyglycolic acid. Surgery 1981;89:672-7.
380. Dougherty SH, Simmons RL. The biology and practice of surgical drains. Part II. Curr Probl Surg 1992;29(9):635-730.
381. Cruse PJE. Wound infections: epidemiology and clinical characteristics in surgical infectious disease. In: Howard RJ, Simmons RL, eds. Surgical infectious diseases. 2nd ed. Norwalk (CT): Appleton and Lange; 1988. p. 319-29.
382. Drinkwater CJ, Neil MJ. Optimal timing of wound drain removal following total joint arthroplasty. J Arthroplasty 1995;10(2):185-9.
383. Tollofsrud SG, Gundersen Y, Andersen R. Perioperative hypothermia. Acta Anaesthesiol Scand 1984;28:511-5.
384. Sessler DI. Mild perioperative hypothermia. N Engl J Med 1997;336(24):1730-7.
385. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996;334(19):1209-15.
386. Hunt TK, Hopf HW. Wound healing and wound infection. What surgeons and anesthesiologists can do. Surg Clin North Am 1997;77:587-606.
387. Wenisch C, Narzt E, Sessler DI, Parschalk B, Lenhardt R, Kurz A, et al. Mild intraoperative hypothermia reduces production of reactive oxygen intermediates by polymorphonuclear leukocytes. Anesth Analg 1996;82:810-6.
388. Jonsson K, Hunt TK, Mathes SJ. Oxygen as an isolated variable influences resistance to infection. Ann Surg 1988;208:783-7.
389. Jonsson K, Jensen JA, Goodson WH 3d, West JM, Hunt TK. Assessment of perfusion in postoperative patients using tissue oxygen measurements. Br J Surg 1987;74:263-7.
390. Chang N, Goodson WH 3d, Gottrup F, Hunt TK. Direct measurement of wound and tissue oxygen tension in postoperative patients. Ann Surg 1983;197:470-8.
391. Knighton DR, Halliday B, Hunt TK. Oxygen as an antibiotic. The effect of inspired oxygen on infection. Arch Surg 1984;119:199-204.
392. Ikeda T, Tayefeh F, Sessler DI, Kurz A, Plattner O, Petschnigg B, et al. Local radiant heating increases subcutaneous oxygen tension. Am J Surg 1998;175:33-7.
393. DuMortier JJ. The resistance of healing wounds to infection. Surg Gynecol Obstet 1933;56:762-6.
394. Morain WD, Colen LB. Wound healing in diabetes mellitus. Clin Plast Surg 1990;17:493-501.
395. American Hospital Association. Infection control in the hospital. Chicago: American Hospital Association; 1979. p. 161-2.
396. Castle M, Ajemian E. Hospital infection control: principles and practice. New York: John Wiley & Sons; 1987. p. 114-6.
397. Centers for Disease Control. Isolation techniques for use in hospitals. Washington: Public Health Service Publication; 1970.
398. Kravitz M. Outpatient wound care. Crit Care Nurs Clin North Am 1996;8(2):217-33.
399. Condon RE, Schulte WJ, Malangoni MA, Anderson-Teschendorf MJ. Effectiveness of a surgical wound surveillance program. Arch Surg 1983;118:303-7.
400. Haley RW, Culver DH, White JW, Morgan WM, Emori TG, Munn VP. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. Am J Epidemiol 1985;121:182-205.
401. Lennard ES, Hargiss CO, Schoenknecht FD. Postoperative wound infection surveillance by use of bacterial contamination categories. Am J Infect Control 1985;13:147-53.
402. Olson MM, Lee JT Jr. Continuous, 10-year wound infection surveillance. Results, advantages, and unanswered questions. Arch Surg 1990;125:794-803.
403. Olson M, O'Connor MO, Schwartz ML. Surgical wound infections. A 5-year prospective study of 20,193 wounds at the Minneapolis VA Medical Center. Ann Surg 1984;199:253-9.
404. Weigelt JA. Risk of wound infections in trauma patients. Am J Surg 1985;150:782-4.
405. Weigelt JA, Haley RW, Seibert B. Factors which influence the risk of wound infection in trauma patients. J Trauma 1987;27(7):774-81.
406. Anonymous. New classification of physical status. Anesthesiology 1963;24:-111.
407. Owens WD. ASA physical status classification: a study on consistency of ratings. Anesthesiology 1978;49:239-43.
408. National Nosocomial Infections Surveillance System. Nosocomial infection rates for interhospital comparison: limitations and possible solutions. A report from the National Nosocomial Infections Surveillance (NNIS) System. Infect Control Hosp Epidemiol 1991;12:609-21.
409. Cardo DM, Falk PS, Mayhall CG. Validation of surgical wound surveillance. Infect Control Hosp Epidemiol 1993;14:211-5.
410. Horan T, Gaynes R, Culver D, National Nosocomial Infections Surveillance (NNIS) System, CDC. Development of predictive risk factors for nosocomial surgical site infections (SSI) [abstract]. Infect Control Hosp Epidemiol 1994;15(suppl):P46(M72).
411. Nichols RL, Smith JW, Klein DB, Trunkey DD, Cooper RH, Adinolfi MF, et al. Risk of infection after penetrating abdominal

trauma. N Engl J Med 1984;311:1065-70.
412. Nichols RL, Smith JW, Robertson GD, Muzik AC, Pearce P, Ozmen V, et al. Prospective alterations in therapy for penetrating abdominal trauma. Arch Surg 1993;128:55-64.
413. Horan TC, Culver DH, Gaynes RP, National Nosocomial Infections Surveillance (NNIS) System. Results of a multicenter study on risk factors for surgical site infections (SSI) following C-section (CSEC) [abstract]. Am J Infect Control 1996;24:84.
414. Roy MC, Herwaldt LA, Embrey R, Kuhns K, Wenzel RP, Perl TM. Does the NNIS risk index (NRI) predict which patients develop wound infection (SWI) after cardiothoracic (CT) surgery? [abstract]. 34th Interscience Conference on Antimicrobial Agents and Chemotherapy 1994; Orlando, FL:196.
415. Lee TB. Surveillance in acute care and nonacute care settings: current issues and concepts. Am J Infect Control 1997;25(2):121-4.
416. Lee JT. Wound infection surveillance. Infect Dis Clin North Am 1992;6(3):643-56.
417. Mead PB, Pories SE, Hall P, Vacek PM, Davis JH Jr, Gamelli RL. Decreasing the incidence of surgical wound infections. Validation of a surveillance-notification program. Arch Surg 1986;121:458-61.
418. Kerstein M, Flower M, Harkavy LM, Gross PA. Surveillance for postoperative wound infections: practical aspects. Am Surg 1978;44:210-4.
419. Poulsen KB, Jepsen OB. Failure to detect a general reduction of surgical wound infections in Danish hospitals. Dan Med Bull 1995;42:485-8.
420. Haley RW, Schaberg DR, McClish DK, Quade D, Crossley KB, Culver DH, et al. The accuracy of retrospective chart review in measuring nosocomial infection rates. Results of validation studies in pilot hospitals. Am J Epidemiol 1980;111(5):516-33.
421. Mulholland SG, Creed J, Dierauf LA, Bruun JN, Blakemore WS. Analysis and significance of nosocomial infection rates. Ann Surg 1974;180:827-30.
422. Wenzel RP, Osterman CA, Hunting KJ, Gwaltney JM Jr. Hospital-acquired infections. I. Surveillance in a university hospital. Am J Epidemiol 1976;103:251-60.
423. Simchen E, Shapiro JM, Michel J, Sacks T. Multivariate analysis of determinants of postoperative wound infection: a possible basis for intervention. Rev Infect Dis 1981;3(4):678-82.
424. Collier C, Miller DP, Borst M. Community hospital surgeon-specific infection rates. Infect Control 1987;8(6):249-54.
425. Ehrenkranz NJ, Shultz JM, Richter EL. Recorded criteria as a "gold standard" for sensitivity and specificity estimates of surveillance of nosocomial infection: a novel method to measure job performance. Infect Control Hosp Epidemiol 1995;16:697-702.
426. Hirschhorn LR, Currier JS, Platt R. Electronic surveillance of antibiotic exposure and coded discharge diagnoses as indicators of postoperative infection and other quality assurance measures. Infect Control Hosp Epidemiol 1993;14:21-8.
427. Simchen E, Wax Y, Pevsner B, Erdal M, Michel J, Modan M, et al. The Israeli Study of Surgical Infections (ISSI): I. Methods for developing a standardized surveillance system for a multicenter study of surgical infections. Infect Control Hosp Epidemiol 1988;9(6):232-40.
428. Burns SJ, Dippe SE. Postoperative wound infections detected during hospitalization and after discharge in a community hospital. Am J Infect Control 1982;10(2):60-5.
429. Laxson LB, Blaser MJ, Parkhurst SM. Surveillance for the detection of nosocomial infections and the potential for nosocomial outbreaks. Am J Infect Control 1984;12(6):318-24.
430. Mertens R, Jans B, Kurz X. A computerized nationwide network for nosocomial infection surveillance in Belgium. Infect Control Hosp Epidemiol 1994;15:171-9.
431. Ehrenkranz NJ. Surgical wound infection occurrence in clean operations; risk stratification for interhospital comparisons. Am J Med 1981;(70):909-14.
432. Baker C, Luce J, Chenoweth C, Friedman C. Comparison of case-finding methodologies for endometritis after cesarean section. Am J Infect Control 1995;23:27-33.
433. Gaynes RP, Horan TC. Surveillance of nosocomial infections. In: Mayhall CG, ed. Hospital Epidemiology and Infection Control. Baltimore:Williams & Wilkins;1996. p. 1017-31.
434. Horan TC, Emori TG. Definitions of key terms used in the NNIS system. Am J Infect Control 1997;25:112-6.
435. Polk BF, Tager IB, Shapiro M, Goren-White B, Goldstein P, Schoenbaum SC. Randomised clinical trial of perioperative cefazolin in preventing infection after hysterectomy. Lancet 1980; 1:437-41.
436. Salem RJ, Johnson J, Devitt P. Short term metronidazole therapy contrasted with povidone-iodine spray in the prevention of wound infection after appendicectomy. Br J Surg 1979;66:430-1.
437. Walsh AL, Roberts FJ, Bryce EA. Post-discharge surveillance of surgical wound infections [letter]. Can J Infect Control 1996;11(1):29.
438. Brown RB, Bradley S, Opitz E, Cipriani D, Pieczarka R, Sands M. Surgical wound infections documented after hospital discharge. Am J Infect Control 1987;15:54-8.
439. Rosendorf LL, Octavio J, Estes JP. Effect of methods of postdischarge wound infection surveillance on reported infection rates. Am J Infect Control 1983;11(6):226-9.
440. Ferraz EM, Ferraz AA, Coelho HS, Pereira Viana V, Sobral SM, Vasconcelos MD, et al. Postdischarge surveillance for nosocomial wound infection: does judicious monitoring find cases? Am J Infect Control 1995;23:290-4.
441. Andenaes K, Amland PF, Lingaas E, Abyholm F, Samdal F, Giercksky KE. A prospective, randomized surveillance study of postoperative wound infections after plastic surgery: a study of incidence and surveillance methods. Plast Reconstr Surg 1995;96(4):948-56.
442. Keeling NJ, Morgan MW. Inpatient and post-discharge wound infections in general surgery. Ann R Coll Surg Engl 1995;77:245-7.
443. Manian FA, Meyer L. Adjunctive use of monthly physician questionnaires for surveillance of surgical site infections after hospital discharge and in ambulatory surgical patients: report of a seven-year experience. Am J Infect Control 1997;25:390-4.
444. Manian FA, Meyer L. Comparison of patient telephone survey with traditional surveillance and monthly physician questionnaires in monitoring surgical wound infections. Infect Control Hosp Epidemiol 1993;14:216-8.
445. Reimer K, Gleed C, Nicolle LE. The impact of postdischarge infection on surgical wound infection rates. Infect Control 1987;8(6):237-40.
446. Sands K, Vineyard G, Platt R. Surgical site infections occuring after hospital discharge. J Infect Dis 1996;173:963-70.
447. Weigelt JA, Dryer D, Haley RW. The necessity and efficiency of wound surveillance after discharge. Arch Surg 1992;127:77-82.
448. Gravel-Tropper D, Oxley C, Memish Z, Garber GE. Underestimation of surgical site infection rates in obstetrics and gynecology. Am J Infect Control 1995;23:22-6.
449. Taylor S, Pearce P, McKenzie M, Taylor GD. Wound infection in total joint arthroplasty: effect of extended wound surveillance on wound infection rates. Can J Surg 1994;37(3):217-20.
450. Hulton LJ, Olmsted RN, Treston-Aurand J, Craig CP. Effect of postdischarge surveillance on rates of infectious complications after cesarean section. Am J Infect Control 1992;20:198-201.
451. Law DJ, Mishriki SF, Jeffery PJ. The importance of surveillance after discharge from hospital in the diagnosis of postoperative wound infection. Ann R Coll Surg Engl 1990;72:207-9.
452. Donovan IA, Ellis D, Gatehouse D, Little G, Grimley R, Armistead

S, et al. One-dose antibiotic prophylaxis against wound infection after appendicectomy: a randomized trial of clindamycin, cefazolin sodium and a placebo. Br J Surg 1979;66:193-6.
453. Bates T, Down RH, Houghton MC, Lloyd GJ. Topical ampicillin in the prevention of wound infection after appendicectomy. Br J Surg 1974;61:489-92.
454. Centers for Disease Control and Prevention. Evaluation of blunt suture needles in preventing percutaneous injuries among healthcare workers during gynecologic surgical procedures New York City, March 1993-June 1994. MMWR Morb Mortal Wkly Rep 1997;46(2):25-9.
455. Fanning C, Johnston BL, MacDonald S, LeFort-Jost S, Dockerty E. Postdischarge surgical site infection surveillance. Can J Infect Control 1995;10(3):75-9.
456. Holbrook KF, Nottebart VF, Hameed SR, Platt R. Automated postdischarge surveillance for postpartum and neonatal nosocomial infections. Am J Med 1991;91(Suppl 3B):125S-30S.
457. Zoutman D, Pearce P, McKenzie M, Taylor G. Surgical wound infections occuring in day surgery patients. Am J Infect Control 1990;18:277-82.
458. Seaman M, Lammers R. Inability of patients to self-diagnose wound infections. J Emerg Med 1991;9:215-9.
459. Goulbourne IA, Ruckley CV. Operations for hernia and varicose veins in a day-bed unit. Br Med J 1979;2:712-4.
460. Garvey JM, Buffenmyer C, Rycheck RR, Yee R, McVay J, Harger JH. Surveillance for postoperative infections in outpatient gynecologic surgery. Infect Control 1986;7(2):54-8.
461. Flanders E, Hinnant JR. Ambulatory surgery postoperative wound surveillance. Am J Infect Control 1990;18(5):336-9.
462. Gentry LO, Zeluff BJ, Cooley DA. Antibiotic prophylaxis in openheart surgery: a comparison of cefamandole, cefuroxime, and cefazolin. Ann Thorac Surg 1988;46:167-71.
463. Maki DG, Bohn MJ, Stolz SM, Kroncke GM, Archer CW, Myerowitz PD. Comparitive study of cefazolin, cefamandole, and vancomycin for surgical prophylaxis in cardiac and vascular operations. A double-blind randomized trial. J Thorac Cardiovasc Surg 1992;104:1423-34.
464. Haines SJ, Walters BC. Antibiotic prophylaxis for cerebrospinal fluid shunts: a metanalysis. Neurosurgery 1994;34(1):87-92.
465. Langley JM, LeBlanc JC, Drake J, Milner R. Efficacy of antimicrobial prophylaxis in placement of cerebrospinal fluid shunts: meta-analysis. Clin Infect Dis 1993;17:98-103.
466. Starr MB, Lally JM. Antimicrobial prophylaxis for ophthalmic surgery. Surv Ophthalmol 1995;39:485-501.
467. Gatell JM, Riba J, Lozano ML, Mana J, Ramon R, Garcia Sanmiguel J. Prophylactic cefamandole in orthopaedic surgery. J Bone Joint Surg Am 1984;66:1219-22.
468. Kent KC, Bartek S, Kuntz KM, Anninos E, Skillman JJ. Prospective study of wound complications in continuous infrainguinal incisions after lower limb arterial reconstruction: incidence, risk factors, and cost. Surgery 1996;119(4):378-83.
469. Wymenga AB, van Horn JR, Theeuwes A, Muytjens HL, Slooff TJ. Perioperative factors associated with septic arthritis after arthroplasty. Prospective multicenter study of 362 knee and 2,651 hip operations. Acta Orthop Scand 1992;63(6):665-71.
470. Stambough JL, Beringer D. Postoperative wound infections complicating adult spine surgery. J Spinal Disord 1992;5(3):277-85.
471. Trippel SB. Antibiotic-impregnated cement in total joint arthroplasty. J Bone Joint Surg Am 1986;68A:1297-302.
472. Nungu KS, Olerud C, Rehnberg L, Larsson S, Nordell P, Allvin I, et al. Prophylaxis with oral cefadroxil versus intravenous cefuroxime in trochanteric fracture surgery. A clinical multicentre study. Arch Orthop Trauma Surg 1995;114(6):303-7.
473. Norden CW. Antibiotic prophylaxis in orthopedic surgery. Rev Infect Dis 1991;13(Suppl 10):S842-6.
474. Aznar R, Mateu M, Miro JM, Gatell JM, Gimferrer JM, Aznar E, et al. Antibiotic prophylaxis in non-cardiac thoracic surgery: cefazolin versus placebo. Eur J Cardiothorac Surg 1991;5:515-8.
475. Cant PJ, Smyth S, Smart DO. Antibiotic prophylaxis is indicated for chest stab wounds requiring closed tube thoracostomy. Br J Surg 1993;80:464-6.
476. Pitt HA, Postier RG, MacGowan AW, Frank LW, Surmak AJ, Sitzman JV, et al. Prophylactic antibiotics in vascular surgery. Topical, systemic, or both? Ann Surg 1980;192:356-64.
477. Kaiser AB, Clayson KR, Mulherin JL Jr, Roach AC, Allen TR, Edwards WH, et al. Antibiotic prophylaxis in vascular surgery. Ann Surg 1978;188:283-9.
478. Bauer T, Vennits B, Holm B, Hahn-Pedersen J, Lysen D, Galatius H, et al. Antibiotic prophylaxis in acute nonperforated appendicitis. The Danish Multicenter Study Group II. Ann Surg 1989;209:307-11.
479. Skipper D, Corder AP, Karran SJ. A randomized prospective study to compare ceftizoxime with cephradine as single dose prophylaxis in elective cholecystectomy. J Hosp Infect 1991;17:303-6.
480. Kaufman Z, Engelberg M, Eliashiv A, Reiss R. Systemic prophylactic antibiotics in elective biliary surgery. Arch Surg 1984;119:1002-4.
481. Grant MD, Jones RC, Wilson SE, Bombeck CT, Flint LM, Jonasson O, et al. Single dose cephalosporin prophylaxis in high-risk patients undergoing surgical treatment of the biliary tract. Surg Gynecol Obstet 1992;174:347-54.
482. Lewis RT, Goodall RG, Marien B, Park M, Lloyd-Smith W, Wiegand FM. Biliary bacteria, antibiotic use, and wound infection in surgery of the gallbladder and common bile duct. Arch Surg 1987;122:44-7.
483. Saltzstein EC, Mercer LC, Peacock JB, Dougherty SH. Outpatient open cholecystectomy. Surg Gynecol Obstet 1992;174(3):173-5.
484. Meijer WS, Schmitz PI, Jeekel J. Meta-analysis of randomized, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. Br J Surg 1990;77:283-90.
485. Kaiser AB, Herrington JL Jr, Jacobs JK, Mulherin JL Jr, Roach AC, Sawyers JL. Cefoxitin versus erythromycin, neomycin, and cefazolin in colorectal operations. Importance of the duration of the surgical procedure. Ann Surg 1983;198:525-30.
486. Schoetz DJ Jr, Roberts PL, Murray JJ, Coller JA, Veidenheimer MC. Addition of parenteral cefoxitin to regimen of oral antibiotics for elective colorectal operations. A randomized prospective study. Ann Surg 1990;212:209-12.
487. Edmondson HT, Rissing JP. Prophylactic antibiotics in colon surgery. Arch Surg 1983;118:227-31.
488. Wapnick S, Guinto R, Reizis I, LeVeen HH. Reduction of postoperative infection in elective colon surgery with preoperative administration of kanamycin and erythromycin. Surgery 1979;85:317-21.
489. Washington JA 2d, Dearing WH, Judd ES, Elveback LR. Effect of preoperative antibiotic regimen on development of infection after intestinal surgery. Prospective, randomized, double-blind study. Ann Surg 1974;108:567-72.
490. Maki DG, Aughey DR. Comparative study of cefazolin, cefoxitin, and ceftizoxime for surgical prophylaxis in colo-rectal surgery. J Antimicrob Chemother 1982;10(Suppl C):281-7.
491. Rotman N, Hay JM, Lacaine F, Fagniez PL, The Association de Recherche en Chirurgie Cooperative Group. Prophylactic antibiotherapy in abdominal surgery. First- vs third-generation cephalosporins. Arch Surg 1989;124:323-7.
492. Lewis RT, Allan CM, Goodall RG, Marien B, Park M, Lloyd-Smith W, et al. Cefamandole in gastroduodenal surgery: a controlled, prospective, randomized, double-blind study. Can J Surg 1982;25(5):561-3.

493. McArdle CS, Morran CG, Anderson JR, Pettit L, Gemmell CG, Sleigh JD, et al. Oral ciprofloxacin as prophylaxis in gastroduodenal surgery. J Hosp Infect 1995;30(3):211-6.
494. Grandis JR, Vickers RM, Rihs JD, Yu VL, Johnson JT. Efficacy of topical amoxicillin plus clavulanate/ticarcillin plus clavulanate and clindamycin in contaminated head and neck surgery: effect of antibiotic spectra and duration of therapy. J Infect Dis 1994;170:729-32.
495. Johnson JT, Yu VL, Myers EN, Wagner RL. An assessment of the need for gram-negative bacterial coverage in antibiotic prophylaxis for oncological head and neck surgery. J Infect Dis 1987;155(2):331-3.
496. Elledge ES, Whiddon RG Jr, Fraker JT, Stambaugh KI. The effects of topical oral clindamycin antibiotic rinses on the bacterial content of saliva on healthy human subjects. Otolaryngol Head Neck Surg 1991;105:836-9.
497. Johnson JT, Yu VL, Myers EN, Wagner RL, Sigler BA. Cefazolin vs moxalactam? A double-blind randomzied trial of cephalosporins in head and neck surgery.Arch Otolaryngol Head Neck Surg 1986;112:151-3.

Selected Readings

Association of Operating Room Nurses. Standards, recommended practices, guidelines. Denver: Association of Operating Room Nurses; 1999.

Larson EL. APIC guideline for handwashing and hand antisepsis in health care settings. Am J Infect Control 1995;23:251-69.

Association of Operating Room Nurses. Recommended practices for skin preparation of patients. AORN J 1996;64:813-6.

Rutala WA. APIC guideline for selection and use of disinfectants. Am J Infect Control 1990;18:99-117.

Favero MS, Bond W. Sterilization, disinfection, and antisepsis in the hospital. In: Balows A, Haugler WJ Jr, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of clinical microbiology. 5th ed. Washington (DC): American Society for Microbiology; 1991. p. 183-200.

Association for the Advancement of Medical Instrumentation. Flash sterilization: steam sterilization of patient care items for immediate use (ANSI/AAMI ST37-1996). Arlington (VA): Association for the Advancement of Medical Instrumentation; 1996.

American Institute of Architects Committee. Guidelines for design and construction of hospital and health care facilities. Washington: American Institiute of Architects Press; 1996.

Association for the Advancement of Medical Instrumentation. Selection of surgical gowns and drapes in health care facilities (AAMI TIR No. 11-1994). Arlington (VA): Association for the Advancement of Medical Instrumentation; 1994.

Platt R. Guidelines for perioperative antibiotic prophylaxis. In: Abrutyn E, Goldmann DA, Scheckler WE, eds. Saunders infection control reference service. Philadelphia: W.B. Saunders Co; 1997. p. 229-34.

Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 1992;326:281-6.

Wong ES. Surgical site infections. In: Mayhall CG, ed. Hospital Epidemiology and Infection Control. Baltimore: Williams & Wilkins; 1996. p. 154-74.

Hochberg J, Murray GF. Principles of operative surgery: antisepsis, technique, sutures, and drains. In: Sabiston DC Jr, ed. Textbook of surgery: the biological basis of modern surgical practice. 15 ed. Philadelphia: W.B. Saunders Co; 1997. p. 253-63.

Roy MC. Surgical-site infections after coronary artery bypass graft surgery: discriminating site-specific risk factors to improve prevention efforts. Infect Control Hosp Epidemiol 1998;19:229-33.

Herwaldt LA, Pottinger J, Coffin SA. Nosocomial infections associated with anesthesia. In: Mayhall CG, ed. Hospital epidemiology and infection control. Baltimore: Williams & Wilkins; 1996. p. 655-75.

Gaynes RP, Horan TC. Surveillance of nosocomial infections. In: Mayhall CG, ed. Hospital epidemiology and infection control. Baltimore: Williams & Wilkins; 1996. p. 1017-31.

Roy MC, Perl TM. Basics of surgical-site infection surveillance. Infect Control Hosp Epidemiol 1997;18:659-68.

Lee JT. Surgical wound infections: surveillance for quality improvement. In: Fry DE, ed. Surgical Infections. Boston: Little, Brown and Co; 1995. p. 145-59.

Meier PA. Infection control issues in same-day surgery. In: Wenzel RP, ed. Prevention and control of nosocomial infections. 3rd ed. Baltimore: Williams & Wilkins; 1997. p. 261-82.

Burke JP. Infections of cardiac and vascular prostheses. In: Bennett JV, Brachman PS, eds. Hospital infections. 4th ed. Philadelphia: Lippincott-Raven; 1998. p. 599-612.

Lew DP, Waldvogel FA. Infections of skeletal prostheses. In: Bennett JV, Brachman PS, eds. Hospital Infections. 4th ed. Philadelphia: Lippincott-Raven; 1998. p. 613-20.

Nafziger DA, Saravolatz LD. Infection in implantable prosthetic devices. In: Wenzel RP, ed. Prevention and control of nosocomial infections. 3rd ed. Baltimore: Williams & Wilkins; 1997. p. 889-923.

CE CONTINUING EDUCATION EXAMINATION ON THE "GUIDELINE FOR PREVENTION OF SURGICAL SITE INFECTION, 1999"

The Centers for Disease Control and Prevention (CDC) is accredited as a provider of continuing education by the International Association for Continuing Education and Training (IACET) and the Accreditation Council for Continuing Medical Education (ACCME) and the American Nurses Credentialing Center's Commission on Accreditation. This learner-paced study package has been structured according to IACET's Criteria and Guidelines and ACCME's Essentials and Standards. The CDC designates this educational activity for a maximum of .15 continuing education units (CEUs), 1.5 category 1 credit (CME) toward the American Medical Association's Physician's Recognition Award, or 1.8 contact hours of continuing nurses education (CNE) credit.

INSTRUCTIONS FOR CREDIT

1. To receive credit, read the objectives and guideline, then complete and return the examination answer form either electronically *(http://www.cdc.gov/ncidod/hip/)* or by post to: SSI Guideline Evaluation Activity, Hospital Infections Program, Mailstop E69, Centers for Disease Control and Prevention, 1600 Clifton Road, NE, Atlanta, GA 30333.
2. Allow 45 days for processing the application and awarding credit. A certificate of completion will be mailed to you.
3. There is no fee for participating in this activity.
4. The deadline for applying for CEU, CME, or CNE for this learning activity is April 15, 2000.

OBJECTIVES

1. Describe the frequency of surgical site infections in hospitalized patients.
2. List the most frequently occurring pathogens associated with surgical site infections and list potential reservoirs of infection.
3. List three intrinsic factors associated with increased risk of surgical site infection.
4. Identify three preoperative practices that have been shown to reduce the risk of surgical site infection.
5. Identify three intraoperative practices that, although not proven, may reduce the risk of surgical site infection.
6. Define the criteria for surgical site infections used for surveillance purposes.
7. Describe inpatient, outpatient, and postdischarge methods of surgical site infection surveillance.
8. List three variables used to stratify the risks associated with development of surgical site infection.

EXAMINATION QUESTIONS (Circle the answer[s] on the answer form)

Part I.

1. SSIs are the most frequently occurring nosocomial infection among all hospitalized patients. T F
2. Most SSIs are confined to the incision. T F
3. When an SSI contributes to a patient's death, it is usually a serious infection involving organs or spaces accessed during the operation. T F
4. According to NNIS system data, the most frequently isolated pathogens in rank order from SSI are:
   a. *Escherichia coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and coagulase-negative staphylococci
   b. *Staphylococcus aureus*, coagulase-negative staphylococci, *Enterococcus* spp., and *Escherichia coli*
   c. *Staphylococcus aureus*, *Enterococcus* spp., *Escherichia coli*, and *Pseudomonas aeruginosa*
   d. *Klebsiella* spp., *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and coagulase-negative staphylococci
5. The risk of SSI is related to the interaction between the dose of bacterial contamination, the virulence of the organism, and the resistance of the host patient. T F
6. For most SSIs, which of the following is the primary source of pathogens
   a. Operating room air
   b. Surgical team members
   c. Contaminated instruments
   d. Patient's endogenous flora
7. Which of the following patient characteristics has been associated with increased SSI risk?
   a. Obesity (>20% ideal body weight)
   b. Coincident remote site infection
   c. Cigarette smoking
   d. All of the above
8. The association between SSI risk and receipt of steroids or immunosuppressive drugs is unresolved. T F
9. Preoperative antiseptic showering has been shown to reduce skin microbial colony counts and reduce SSI rates. T F
10. The surgical scrub must be performed for a duration of 10 minutes with an appropriate antiseptic. T F
11. Timing of antimicrobial prophylaxis should be such that an adequate bactericidal concentration of the drug is established in serum and tissues by the time the skin is incised. T F
12. Flash sterilization is acceptable for the routine reprocessing of surgical instruments that are in short supply. T F
13. Prophylactic antimicrobial agents should be extended for at least 72 hours postoperatively. T F
14. Operating rooms should be maintained at negative pressure with respect to corridors and adjacent areas. T F
15. An incision closed primarily should be protected with a sterile dressing for 24 to 48 hours postoperatively. T F
16. Surgical surveillance efforts should be targeted toward high-risk procedures. T F
17. Which of the following practices are identified as unresolved issues with respect to their potential for reducing SSI rates? (Select all that apply.)
   a. Providing coded surgeon-specific data to the infection control committee
   b. Covering a scrub suit when out of the operating suite
   c. Using tacky mats at the entrance to the operating suite
   d. Using ultraviolet radiation in the operating room
18. Which of the following practices is *not* considered good surgical technique?
   a. Gentle handling of tissues
   b. Maintaining effective hemostasis
   c. Placing of a drain through the main surgical incision
   d. Minimizing the amount of devitalized tissue
19. Infection control professionals should routinely assign the surgical wound classification. T F

ANSWER FORM

Continuing Education Examination on the "Guideline for Prevention of Surgical Site Infection, 1999." There is no fee for applying for CEU, CME or CNE for this learning activity; deadline for application is April 15, 2000.

Part I.

1.	T	F			6.	a	b	c	d	11.	T	F			16.	T	F		
2.	T	F			7.	a	b	c	d	12.	T	F			17.	a	b	c	d
3.	T	F			8.	T	F			13.	T	F			18.	a	b	c	d
4.	a	b	c	d	9.	T	F			14.	T	F			19.	T	F		
5.	T	F			10.	T	F			15.	T	F							

Part II.

The following questions will not be included in your examination score, but your answers are critical to help us evaluate who reads and implements the guideline.

20. Which of the following best describes your profession?
    - ❑ Physician
      Check one: ❑ Surgeon ❑ Anesthesiologist ❑ Infectious Disease ❑ OB/GYN ❑ Other
    - ❑ Infection Control Professional (includes Infection Control Nurse)
    - ❑ Nurse
      Check one: ❑ Operating Room Nurse ❑ Other
    - ❑ Operating Room Technician
    - ❑ Physician's Assistant
    - ❑ Pharmacist
    - ❑ Other (specify) _____
21. Are you responsible for managing surgical patients?
    ❑ Yes ❑ No
22. Are you responsible for developing policies for prevention and control of nosocomial surgical site infections?
    ❑ Yes ❑ No
23. Are you responsible for directing or performing surveillance of surgical site infections?
    ❑ Yes ❑ No
24. In which of the following settings do you perform the responsibilities identified in items 21 to 23 above? (Check all that apply)
    - ❑ Hospital-based (Check all that apply): ❑ Inpatient surgery ❑ Outpatient surgery
    - ❑ Free-standing surgery center
    - ❑ Home care services
25. How long did it take you to complete this learning activity?
    - ❑ Less than 90 minutes
    - ❑ 90 minutes
    - ❑ Greater than 90 minutes

Part III.

The following questions will not be included in your examination score, but will help us assess your perceptions of how well the learning objectives were met and how readable and easily understood the material was.

	1 Strongly Agree	2 Agree	3 Neither Agree nor Disagree	4 Disagree	5 Strongly Disagree
26. All learning objectives were relevant to the SSI Guideline.	1	2	3	4	5
27. I understood what the authors were trying to say.	1	2	3	4	5
28. I was able to interpret the tables and figure.	1	2	3	4	5
29. Overall, the presentation of the guideline enhanced my ability to read and understand it.	1	2	3	4	5

APPLICATION FOR CONTINUING EDUCATION CREDIT

Name: _____

Mailing address: _____

_____

Daytime phone number: _____

Type of credit: ❑ CEU ❑ CME ❑ CNE

Date of application: _____

Signature: _____

Return to: SSI Guideline Evaluation, Hospital Infections Program/CDC, Mailstop E69, 1600 Clifton Road, NE, Atlanta, GA 30333.

EXHIBIT DX5

TO DECLARATION OF MARY S. YOUNG IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION TO EXCLUDE OPINIONS AND TESTIMONY OF RICHARD WENZEL, M.D.

Education and debate

How to read a paper

Getting your bearings (deciding what the paper is about)

Trisha Greenhalgh

The science of "trashing" papers

It usually comes as a surprise to students to learn that some (perhaps most) published articles belong in the bin, and should certainly not be used to inform practice.[1] The first box shows some common reasons why papers are rejected by peer reviewed journals.

Most papers now appearing in medical journals are presented more or less in standard IMRAD format: Introduction (why the authors decided to do this research), Methods (how they did it, and how they analysed their results), Results (what they found), and Discussion (what the results mean). If you are deciding whether a paper is worth reading, you should do so on the design of the methods section and not on the interest of the hypothesis, the nature or potential impact of the results, or the speculation in the discussion.

Critical appraisal

The assessment of methodological quality (critical appraisal) has been covered in detail in many textbooks on evidence based medicine,[2-6] and in Sackett and colleagues' Users' Guides to the Medical Literature in *JAMA*.[7-21] If you are an experienced journal reader, the structured checklists produced by these authors will be largely self explanatory. If you are not, try these preliminary questions.

Question 1: Why was the study done, and what clinical question were the authors addressing?

The introductory sentence of a research paper should state, in a nutshell, what the background to the research is. For example, "Grommet insertion is a common procedure in children, and it has been suggested that not all operations are clinically necessary." This statement should be followed by a brief review of the published literature.

Unless it has already been covered in the introduction, the hypothesis which the authors have decided to test should be clearly stated in the methods section of the paper. If the hypothesis is presented in the negative, such as "the addition of metformin to maximal dose sulphonylurea therapy will not improve the control of type 2 diabetes," it is known as a null hypothesis.

The authors of a study rarely actually believe their null hypothesis when they embark on their research. Being human, they have usually set out to show a difference between the two arms of their study. But the way scientists do this is to say, "Let's assume there's no difference; now let's try to disprove that theory." If you adhere to the teachings of Karl Popper, this hypothetico-deductive approach (setting up falsifiable hypotheses which you then proceed to test) is the very essence of the scientific method.[22]

Summary points

Many papers published in medical journals have potentially serious methodological flaws

When deciding whether a paper is valid and relevant to your practice, first establish what specific clinical question it addressed

Questions to do with drug treatment or other medical interventions should be addressed by double blind, randomised controlled trials

Questions about prognosis require longitudinal cohort studies, and those about causation require either cohort or case-control studies

Case reports, though methodologically weak, can be produced rapidly and have a place in alerting practitioners to adverse drug reactions

Why were papers rejected for publication?

- The study did not address an important scientific issue
- The study was not original (someone else had already done the same or a similar study)
- The study did not actually test the authors' hypothesis
- A different type of study should have been done
- Practical difficulties (in recruiting subjects, for example) led the authors to compromise on the original study protocol
- The sample size was too small
- The study was uncontrolled or inadequately controlled
- The statistical analysis was incorrect or inappropriate
- The authors drew unjustified conclusions from their data
- There is a significant conflict of interest (one of the authors, or a sponsor, might benefit financially from the publication of the paper and insufficient safeguards were seen to be in place to guard against bias)
- The paper is so badly written that it is incomprehensible

This is the second of 10 articles introducing non-experts to finding medical articles and assessing their value

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BMJ 1997;315:243–6

Terms used to describe design features of clinical research studies

Parallel group comparison—Each group receives a different treatment, with both groups being entered at the same time; results are analysed by comparing groups

Paired (or matched) comparison—Subjects receiving different treatments are matched to balance potential confounding variables such as age and sex; results are analysed in terms of differences between subject pairs

Within subject comparison—Subjects are assessed before and after an intervention and results analysed in terms of changes within the subjects

Single blind—Subjects did not know which treatment they were receiving

Double blind—Neither did the investigators

Crossover—Each subject received both the intervention and control treatments (in random order), often separated by a washout period with no treatment

Placebo controlled—Control subjects receive a placebo (inactive pill) which should look and taste the same as the active pill. Placebo (sham) operations may also be used in trials of surgery

Factorial design—A study which permits investigation of the effects (both separately and combined) of more than one independent variable on a given outcome (for example, a 2 × 2 factorial design tested the effects of placebo, aspirin alone, streptokinase alone, or aspirin plus streptokinase in acute heart attack[23])

Question 2: What type of study was done?

First, decide whether the paper describes a primary study, which reports research first hand, or a secondary (or integrative) one, which attempts to summarise and draw conclusions from primary studies. Primary studies, the stuff of most published research in medical journals, usually fall into one of three categories:

- Experiments, in which a manoeuvre is performed on an animal or a volunteer in artificial and controlled surroundings;
- Clinical trials, in which an intervention, such as a drug treatment, is offered to a group of patients who are then followed up to see what happens to them; or
- Surveys, in which something is measured in a group of patients, health professionals, or some other sample of individuals.

The second box shows some common jargon terms used in describing study design.

Secondary research is made up of:

- Overviews, which may be divided into:
  [Non-systematic] reviews, which summarise primary studies;
  Systematic reviews, which do this according to a rigorous and predefined methodology; and
  Meta-analyses, which integrate the numerical data from more than one study.
- Guidelines, which draw conclusions from primary studies about how clinicians should be behaving.
- Decision analyses, which use the results of primary studies to generate probability trees to be used by health professionals and patients in making choices about clinical management.[24-26]
- Economic analyses, which use the results of primary studies to say whether a particular course of action is a good use of resources.

Question 3: Was this design appropriate to the research?

This question is best addressed by considering what broad field of research is covered by the study. Most research studies are concerned with one or more of the broad fields shown in the box below.

Randomised controlled trials

In a randomised controlled trial, participants are randomly allocated by a process equivalent to the flip of a coin to either one intervention (such as a drug) or another (such as placebo treatment or a different drug). Both groups are followed up for a specified period and analysed in terms of outcomes defined at the outset (death, heart attack, serum cholesterol level, etc). Because, on average, the groups are identical apart from the intervention, any differences in outcome are, in theory, attributable to the intervention.

Some trials comparing an intervention group with a control group are not randomised trials. Random allocation may be impossible, impractical, or unethical—for example, in a trial to compare the outcomes of childbirth at home and in hospital. More commonly, inexperienced investigators compare one group (such as patients on ward A) with another (such as patients on ward B). With such designs, it is far less likely that the two groups can reasonably be compared with one another on a statistical level.

A randomised controlled trial should answer questions such as the following:

- Is this drug better than placebo or a different drug for a particular disease?
- Is a leaflet better than verbal advice in helping patients make informed choices about the treatment options for a particular condition?

It should be remembered, however, that randomised trials have several disadvantages (see box).[27] Remember, too, that the results of a trial may have limited applicability as a result of exclusion criteria (rules about who may not be entered into the study), inclusion bias (selection of subjects from a group unrepresentative of everyone with the condition), refusal of certain patient groups to give consent to be included in the trial,[28] analysis of only predefined "objective" endpoints which may exclude important qualitative aspects of the intervention, and publication bias (the selective publication of positive results).[29]

Broad fields of research

- *Therapy:* testing the efficacy of drug treatments, surgical procedures, alternative methods of service delivery, or other interventions. Preferred study design is randomised controlled trial
- *Diagnosis:* demonstrating whether a new diagnostic test is valid (can we trust it?) and reliable (would we get the same results every time?). Preferred study design is cross sectional survey in which both the new test and the gold standard are performed
- *Screening:* demonstrating the value of tests which can be applied to large populations and which pick up disease at a presymptomatic stage. Preferred study design is cross sectional survey
- *Prognosis:* determining what is likely to happen to someone whose disease is picked up at an early stage. Preferred study design is longitudinal cohort study
- *Causation:* determining whether a putative harmful agent, such as environmental pollution, is related to the development of illness. Preferred study design is cohort or case-control study, depending on how rare the disease is, but case reports may also provide crucial information

There is now a recommended format for reporting randomised controlled trials in medical journals.[30] You should try to follow it if you are writing one up yourself.

Cohort studies

In a cohort study, two (or more) groups of people are selected on the basis of differences in their exposure to a particular agent (such as a vaccine, a drug, or an environmental toxin), and followed up to see how many in each group develop a particular disease or other outcome. The follow up period in cohort studies is generally measured in years (and sometimes in decades), since that is how long many diseases, especially cancer, take to develop. Note that randomised controlled trials are usually begun on patients (people who already have a disease), whereas most cohort studies are begun on subjects who may or may not develop disease.

A special type of cohort study may also be used to determine the prognosis of a disease (what is likely to happen to someone who has it). A group of patients who have all been diagnosed as having an early stage of the disease or a positive result on a screening test is assembled (the inception cohort) and followed up on repeated occasions to see the incidence (new cases per year) and time course of different outcomes.

The world's most famous cohort study, which won its two original authors a knighthood, was undertaken by Sir Austin Bradford Hill, Sir Richard Doll, and, latterly, Richard Peto. They followed up 40 000 British doctors divided into four cohorts (non-smokers, and light, moderate, and heavy smokers) using both all cause mortality (any death) and cause specific mortality (death from a particular disease) as outcome measures. Publication of their 10 year interim results in 1964, which showed a substantial excess in both lung cancer mortality and all cause mortality in smokers, with a "dose-response" relation (the more you smoke, the worse your chances of getting lung cancer), went a long way to showing that the link between smoking and ill health was causal rather than coincidental.[31] The 20 year and 40 year results of this momentous study (which achieved an impressive 94% follow up of those recruited in 1951 and not known to have died) illustrate both the perils of smoking and the strength of evidence that can be obtained from a properly conducted cohort study.[32 33]

A cohort study should be used to address clinical questions such as:

- Does high blood pressure get better over time?
- What happens to infants who have been born very prematurely, in terms of subsequent physical development and educational achievement?

Case-control studies

In a case-control study, patients with a particular disease or condition are identified and "matched" with controls (patients with some other disease, the general population, neighbours, or relatives). Data are then collected (for example, by searching back through these people's medical records or by asking them to recall their own history) on past exposure to a possible causal agent for the disease. Like cohort studies, case-control studies are generally concerned with the aetiology of a disease (what causes it) rather than its treatment. They lie lower down the hierarchy of evidence (see below), but this design is usually the only option for studying rare conditions. An important source of difficulty (and potential bias) in a case-control study is the precise definition of who counts as a "case," since one misallocated subject may substantially influence the results. In addition, such a design cannot show causality—the association of A with B in a case-control study does not prove that A has caused B.

A case-control study should be used to address clinical questions such as:

- Does the prone sleeping position increase the risk of cot death (the sudden infant death syndrome)?
- Does whooping cough vaccine cause brain damage?
- Do overhead power cables cause leukaemia?

Randomised controlled trial design

Advantages

- Allows rigorous evaluation of a single variable (effect of drug treatment versus placebo, for example) in a precisely defined patient group (postmenopausal women aged 50-60 years)
- Prospective design (data are collected on events that happen after you decide to do the study)
- Uses hypotheticodeductive reasoning (seeks to falsify, rather than confirm, its own hypothesis)
- Potentially eradicates bias by comparing two otherwise identical groups (but see below)
- Allows for meta-analysis (combining the numerical results of several similar trials at a later date)

Disadvantages

Expensive and time consuming; hence, in practice:

- Many randomised controlled trials are either never done, are performed on too few patients, or are undertaken for too short a period
- Most are funded by large research bodies (university or government sponsored) or drug companies, who ultimately dictate the research agenda
- Surrogate endpoints are often used in preference to clinical outcome measures may introduce "hidden bias," especially through:
- Imperfect randomisation (see above)
- Failure to randomise all eligible patients (clinician only offers participation in the trial to patients he or she considers will respond well to the intervention)
- Failure to blind assessors to randomisation status of patients

Cross sectional surveys

We have probably all been asked to take part in a survey, even if only one asking us which brand of

PETER BROWN

A memorable example of a case report

A doctor notices that two newborn babies in his hospital have absent limbs (phocomelia). Both mothers had taken a new drug (thalidomide) in early pregnancy. The doctor wishes to alert his colleagues worldwide to the possibility of drug related damage as quickly as possible.[35]

toothpaste we prefer. Surveys conducted by epidemiologists are run along the same lines: a representative sample of subjects (or patients) is interviewed, examined, or otherwise studied to gain answers to a specific clinical question. In cross sectional surveys, data are collected at a single time but may refer retrospectively to experiences in the past—such as the study of casenotes to see how often patients' blood pressure has been recorded in the past five years.

A cross sectional survey should be used to address clinical questions such as:

- What is the "normal" height of a 3 year old child?
- What do psychiatric nurses believe about the value of electroconvulsive therapy in severe depression?
- Is it true that half of all cases of diabetes are undiagnosed?

Case reports

A case report describes the medical history of a single patient in the form of a story: "Mrs B is a 54 year old secretary who developed chest pain in June 1995...." Case reports are often run together to form a case series, in which the medical histories of more than one patient with a particular condition are described to illustrate an aspect of the condition, the treatment, or, most commonly these days, adverse reaction to treatment. Although this type of research is traditionally considered to be "quick and dirty" evidence, a great deal of information can be conveyed in a case report that would be lost in a clinical trial or survey .[34]

The hierarchy of evidence

Standard notation for the relative weight carried by the different types of primary study when making decisions about clinical interventions (the "hierarchy of evidence") puts them in the following order[36]:

(1) Systematic reviews and meta-analyses
(2) Randomised controlled trials with definitive results (confidence intervals that do not overlap the threshold clinically significant effect)
(3) Randomised controlled trials with non-definitive results (a point estimate that suggests a clinically significant effect but with confidence intervals overlapping the threshold for this effect)
(4) Cohort studies
(5) Case-control studies
(6) Cross sectional surveys
(7) Case reports.

Thanks to Dr Sarah Walters and Dr Jonathan Elford for advice on this article.

1 Altman DG. The scandal of poor medical research. *BMJ* 1994;308:283-4.
2 Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical epidemiology: a basic science for clinical medicine*. London, Little, Brown, 1991.
3 Sackett DL, Richardson WS, Rosenberg WMC, Haynes RB. *Evidence-based medicine: how to practice and teach EBM*. London: Churchill-Livingstone, 1996.
4 Crombie IM. *The pocket guide to critical appraisal*. London: BMJ Publishing Group, 1996.
5 Fletcher RH, Fletcher SW, Wagner EH. *Clinical epidemiology: the essentials*. 3rd ed. Baltimore: Williams and Williams, 1996.
6 Rose G, Barker DJP. *Epidemiology for the uninitiated*. 3rd ed. London: BMJ Books, 1993.
7 Oxman AD, Sackett DS, Guyatt GH. Users' guides to the medical literature. I. How to get started. *JAMA* 1993;270:2093-5.
8 Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? *JAMA* 1993;270:2598-601.
9 Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. B. What were the results and will they help me in caring for my patients? *JAMA* 1994;271:59-63.
10 Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? *JAMA* 1994;271:389-91.
11 Jaeschke R, Guyatt G, Sackett DL. Users' guides to the medical literature. III. How to use an article about a diagnostic test. B. What were the results and will they help me in caring for my patients? *JAMA* 1994;271:703-7.
12 Levine M, Walter S, Lee H, Haines T, Holbrook A, Moyer V. Users' guides to the medical literature. IV. How to use an article about harm. *JAMA* 1994;271:1615-9.
13 Laupacis A, Wells G, Richardson WS, Tugwell P. Users' guides to the medical literature. V. How to use an article about prognosis. *JAMA* 1994;271:234-7.
14 Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature. VI. How to use an overview. *JAMA* 1994;272:1367-71.
15 Richardson WS, Detsky AS. Users' guides to the medical literature. VII. How to use a clinical decision analysis. A. Are the results of the study valid? *JAMA* 1995;273:1292-5.
16 Richardson WS, Detsky AS. Users' guides to the medical literature. VII. How to use a clinical decision analysis. B. What are the results and will they help me in caring for my patients? *JAMA* 1995;273:1610-3.
17 Hayward RSA, Wilson MC, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. A. Are the recommendations valid? *JAMA* 1995;274:570-4.
18 Wilson MC, Hayward RS, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. B. Will the recommendations help me in caring for my patients? *JAMA* 1995;274:1630-2.
19 Naylor CD, Guyatt GH. Users' guides to the medical literature. XI. How to use an article about a clinical utilization review. *JAMA* 1996;275:1435-9.
20 Drummond MF, Richardson WS, O'Brien BJ, Levine M, Heyland D. Users' guides to the medical literature. XIII. How to use an article on economic analysis of clinical practice. A. Are the results of the study valid? *JAMA* 1997;277:1552-7.
21 O'Brien BJ, Heyland D, Richardson WS, Levine M, Drummond MF. Users' guides to the medical literature. XIII. How to use an article on economic analysis of clinical practice. B. What are the results and will they help me in caring for my patients? *JAMA* 1997;277:1802-6.
22 Popper K. *Conjectures and refutations: the growth of scientific knowledge*. New York: Routledge and Kegan Paul, 1963.
23 Randomised trial of intravenous streptokinase, aspirin, both, or neither among 17187 cases of suspected acute myocardial infarction: ISIS-2. (ISIS-2 Collaborative Group). *Lancet* 1988;ii:349-60.
24 Thornton JG, Lilford RJ, Johnson N. Decision analysis in medicine. *BMJ* 1992;304:1099-103.
25 Thornton JG, Lilford RJ. Decision analysis for medical managers. *BMJ* 1995;310:791-4.
26 Dowie J. "Evidence-based", "cost-effective", and "preference-driven" medicine. *J Health Serv Res Policy* 1996;1:104-13.
27 Bero LA, Rennie D. Influences on the quality of published drug studies. *Int J Health Technology Assessment* 1996;12:209-37.
28 MacIntyre IMC. Tribulations for clinical trials. Poor recruitment is hampering research. *BMJ* 1991;302:1099-100.
29 Easterbrook PJ, Berlin JA, Gopalan R, Matthews DR. Publication bias in clinical research. *Lancet* 1991;337:867-72.
30 Altman D. Better reporting of randomised controlled trials: the CONSORT statement. *BMJ* 1996; 313:570-1.
31 Doll R, Hill AB. Mortality in relation to smoking: ten years' observations on British doctors. *BMJ* 1964;i:1399-414, 1460-7.
32 Doll R, Peto R. Mortality in relation to smoking: ten years' observations on British doctors. *BMJ* 1976;ii:1525-36.
33 Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. *BMJ* 1994;309:901-11.
34 MacNaughton J. Anecdotes and empiricism. *Br J Gen Pract* 1995; 45:571-2.
35 McBride WG. Thalidomide and congenital abnormalities. *Lancet* 1961;ii:1358.
36 Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. *JAMA* 1995;274:1800-4.